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In the Transition to School Routine

During the early school years especially, the transition from unhampered, leisurely vacation days to school routine presents a change which may not be entirely happy in its influence upon the child. In many instances the "rush" to get to school on time may lead to the hurried eating of a skimpy, nutritionally inadequate breakfast.

Yet the dual nutritional needs of childhood make it the more necessary that the morning meal provide an adequate part—not less than one-third—of the day's total food requirement.

A basic breakfast consisting of fruit, cereal, milk, bread and butter is widely recommended by nutritional as well as medical authorities. It makes a notable contribution of virtually every essential nutrient, and in most instances proves calorically adequate.

The appended table shows the combined nutritional values of 1 oz. of cereal (ready to eat or to be cooked), one teaspoonful of sugar, and 4 oz. of whole milk—the usual cereal serving—based on composite averages:

Calories	**205**
Protein	**7 Gm.**
Carbohydrate	**33 Gm.**
Fat	**5 Gm.**
Thiamine	**0.18 mg.**
Riboflavin	**0.30 mg.**
Niacin	**0.84 mg.**
Calcium	**0.16 Gm.**
Iron	**1.29 mg.**

The presence of this seal indicates that all nutritional statements in this advertisement have been found acceptable by the Council on Foods and Nutrition of the American Medical Association.

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The Journal of Pediatrics

VOL. 25 SEPTEMBER, 1944 NO. 3

Original Communications

CHYLOTHORAX IN INFANCY

OBSERVATIONS ON THE ABSORPTION OF VITAMINS A AND D AND ON THE INTRAVENOUS REPLACEMENT OF ASPIRATED CHYLE

GILBERT B. FORBES, M.D.
ST. LOUIS, MO.

CHYLOUS effusion in infancy is rare. In a recent review of the literature Brescia[1] was able to find reports of only ten instances of chylothorax in children under 1 year of age. The case to be presented is that of a 6-week-old infant with spontaneous bilateral chylothorax in which certain observations were made on the characteristics of the chylous fluid; the absorption of vitamins A and D and beta carotene from the gastrointestinal tract into the chylous fluid; and the reintroduction of the aspirated chyle intravenously.

Experimental studies on the absorption of various substances into the thoracic duct are necessarily limited to animal subjects, and it has been demonstrated in the dog that orally administered vitamin A quickly appears in the thoracic duct lymph.[2] The patient with chylothorax, however, becomes a suitable subject for such studies because of the ready availability of large amounts of chyle. Drummond, Bell, and Palmer[3] found that in their patient, a 49-year-old woman with chylothorax and chylous ascites, ingested vitamin A could be recovered quantitatively from the chyle, whereas ingested carotene appeared to the extent of only 20 per cent of the amount fed. A study of the literature revealed no reports concerning the absorption of vitamin D into chyle. Because of the paucity of information available on the role of chyle in the absorption of the fat-soluble vitamins from the gastrointestinal tract, observations on the absorption of vitamins A and D and beta carotene were undertaken in the case herein reported.

From the Department of Pediatrics, Washington University School of Medicine, and the St. Louis Children's Hospital.

I wish to acknowledge the assistance of Dr. A. F. Hartmann in the management of this case and to thank Dr. A. McCoord of Rochester, New York, and Dr. Josef Warkany of Cincinnati, Ohio, for their help in carrying out certain of the vitamin studies.

The problem of maintaining a state of adequate nutrition in this type of patient is an important one, in as much as the withdrawal of large amounts of chyle rich in both fat and protein must be repeatedly carried out in the course of the treatment to relieve and prevent severe dyspnea. Some observations have been made on replacement of the aspirated chyle intravenously. In four of the nine reported cases (all adults) this procedure was of considerable benefit and was thought to have contributed greatly to recovery. In three, there was no definite response observed, and in the remaining two cases sudden death, which was interpreted as an anaphylactic reaction, occurred during the procedure.[4, 5] Since chyle normally enters the systemic circulation by way of the subclavian vein, it seems unlikely that such reactions could occur entirely as a result of anaphylaxis following intravenous administration. In the case to be reported, considerable amounts of the chylous fluid were injected intravenously without ill effects.

CASE REPORT

C. H. (T-272), a 6-week-old white female, was admitted to the St. Louis Children's Hospital on Jan. 25, 1943, because of attacks of dyspnea and cyanosis. She was born at home, weighing 8¾ pounds, after an uneventful delivery; respiration began immediately. She soon began to exhibit episodes of dyspnea and cyanosis and was admitted to another hospital at the age of 3 weeks, where a diagnosis of bilateral bronchopneumonia was made. Despite therapy with oxygen and sulfadiazine these symptoms continued to recur at intervals, and she was brought to the St. Louis Children's Hospital.

On examination the infant appeared well developed and weighed 3,500 Gm.; the temperature was 36.8° C. She was mildly cyanotic and exhibited definite respiratory distress with retraction of the suprasternal and intercostal spaces and a relatively prolonged expiratory phase. There was no evidence of upper respiratory infection and no palpable cervical masses. The breath sounds were moderately suppressed, and many subcrepitant râles could be heard throughout the chest. The cardiac rate was quite rapid, and the heart sounds were muffled; no murmurs could be heard. The remainder of the physical examination was normal. On fluoroscopic examination both lung fields were diffusely hazy. Both leaves of the diaphragm were depressed, and their motion was limited. The cardiac silhouette was normal.

Laboraory findings included a leucocyte count of 11,400, a normal differential, a normal urine, and negative tuberculin and blood Kline reactions.

The clinical picture, in general, resembled that of acute bronchiolitis, a disease which was prevalent at that time. Therapy was begun with sulfapyrazine and steam, and although the patient remained afebrile, respiratory distress continued, and she soon began to exhibit spells of deep cyanosis. Although physical signs in the chest did not change, the fluoroscopic picture became confusing in that relatively clear areas were seen in the left lung field. The possibilities of congenital cystic disease of the lung and of congenital diaphragmatic hernia were considered, and a barium meal was given to rule out the latter. It was not until one week after admission that it was evident that a bilateral effusion was present (Fig. 1). Bilateral thoracentesis, done posteriorly at the lower scapular angle, yielded 40 c.c. of blood-tinged chylous fluid (resembling cream of tomato soup) from the left pleural cavity and 50 c.c. from the right. The various characteristics of this fluid will be described in detail later.

The diagnosis thus having been established as bilateral chylothorax, sulfapyrazine was discontinued and an attempt made to establish the cause of the condition. Study of a fixed preparation of the cellular elements of the fluid failed to reveal tumor cells. Lateral roentgenograms of the chest showed no abnormalities of the mediastinum, and skull films for possible metastatic lesions were normal. Fig. 2 shows the chest just after withdrawal of all available fluid. There was some bronchopneumonia present at this time.

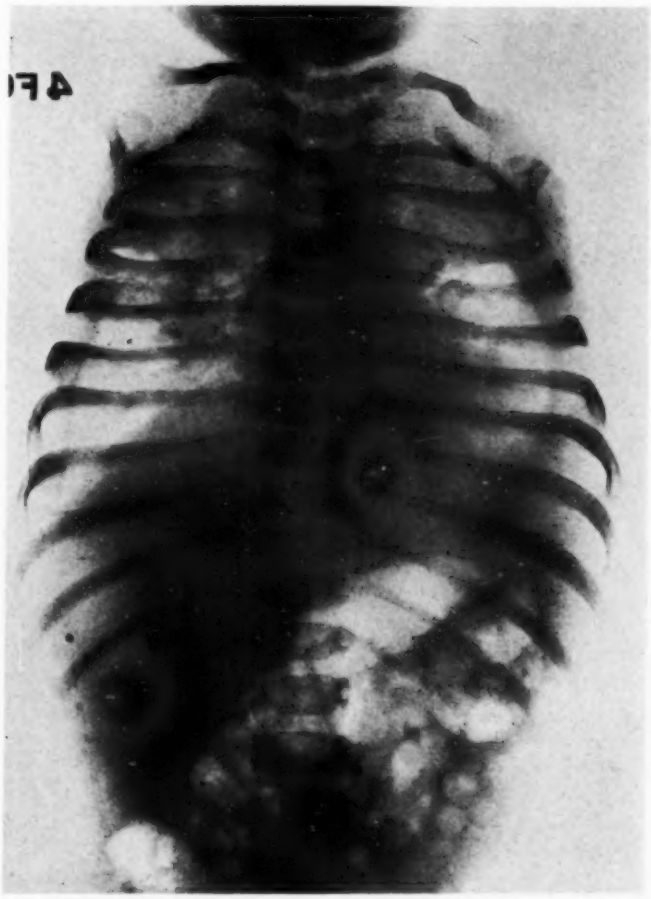

Fig. 1.

The baby's course was quite stormy throughout her two months' hospital stay. She frequently required continuous oxygen therapy for several days at a time, and constant nursing vigilance was necessary because of the frequent occurrence of marked dyspnea and cyanosis. At times she would become sufficiently exhausted to require stimulants.

Therapy consisted of repeated bilateral thoracenteses, which were done whenever the baby's respiratory symptoms warranted relief. Forty-two taps (bilateral)

were done over a period of sixty days; the largest amount of fluid withdrawn from one side at any one time was 180 c.c. The frequency with which these were done varied considerably. On four occasions it was necessary to tap the baby twice in one day to provide relief, and on one occasion thoracentesis was not required for a period of five days. A total of 5,300 c.c. of chyle was removed, 3,600 c.c. from the left pleural cavity and 1,700 c.c. from the right. For some unexplained reason, fluid seemed to accumulate more rapidly and in greater quantity in the left pleural cavity than in the right.

Fig. 2.

Additional therapy consisted of a series of plasma and of whole blood transfusions, and numerous injections of parenteral fluid consisting of dextrose, Amigen,* and lactate-Ringer's solutions. Efforts to maintain the baby's nutrition were of necessity vigorous, for, considering the chylous fluid to contain approximately 2.8 per cent protein (see Table I), she lost by thoracentesis an average of 2.6 Gm. (ap-

*Mead Johnson & Co.

proximately 0.75 Gm. per kilogram of body weight) of protein daily throughout her entire hospital stay. The losses of fat, electrolytes, and water from this source were also considerable. Obviously, the logical method of replacement of these substances was to reintroduce the aspirated chyle intravenously. Therefore, this procedure was adopted to augment the above supportive therapy. Using sterile precautions, chyle was drawn directly from the chest into flasks containing sufficient amounts of sodium citrate to make a final concentration of 0.25 per cent. Small amounts were injected first subcutaneously and then cautiously into a vein, and the baby exhibited no reaction to the procedure. Chyle was then given, in amounts varying from 60 to 100 c.c. per intravenous injection, a total of fourteen times over a period of thirty-eight days without observable reactions of any sort. The fluid was always used within a period of forty-eight hours after withdrawal from the chest.

Despite these measures, the baby became gradually worse, and there was no tendency toward lessening of the formation of chylous effusion. Vigorous efforts to maintain her in an adequate state of nutrition were unsuccessful, and she lost a total of 300 Gm. in weight during her hospital stay. Her temperature remained normal, as did the leucocyte count, until three weeks before death. She then began to exhibit an irregular fever of moderate degree, which may at first have been due to excessive oral protein intake (the formula was fortified with Amigen), but later was due to a bronchopneumonia, for which sulfadiazine was given. The pleural fluid remained sterile, however, and repeated urinalyses were negative.

On April 2, 1943, the baby experienced an episode of cyanosis and apnea which was thought to be due to a tension pneumothorax, for air was recovered on thoracentesis, and she was revived by this procedure. Later that same day she experienced a similar episode and expired.

Autopsy was done twelve hours after death by Dr. Jean Dehlinger. Approximately 100 c.c. of blood-tinged chyle were present in the left pleural cavity, but only a few cubic centimeters in the right. There was bronchopneumonia in all lobes of the lungs, and fresh thrombi were present in several small branches of the pulmonary artery. Careful search, both in the gross and in tissue sections, failed to reveal the thoracic lymph duct or the cisterna chyli. There were no abnormalities of the neck or mediastinum. The heart and pericardium were normal. Additional findings were (1) an unusual degree of insular hyperplasia of the pancreas, (2) focal calcification of the zona reticularis of the adrenal cortex and of the tubular epithelium of the kidney, (3) healed glomerulitis. Examination of the brain was not permitted.

EXPERIMENTAL OBSERVATIONS

Characteristics of the Chylous Fluid.—Once settling of the red blood cells had occurred, the fluid was seen to be a non-viscous, pale yellow, milky liquid which was homogeneous and odorless. An occasional specimen would clot, but such specimens usually contained an appreciable amount of blood. The fluid did not change in appearance on ordinary centrifugation, but on standing at icebox temperature for several days separated a distinct fatty layer resembling cream. Smear of the fluid revealed many lymphocytes, but no bacteria, and it was sterile on culture. It was not until the fatty layer had separated that it was possible to see fat droplets on staining with sudan III. The various characteristics of the chyle, obtained at various times, are listed in Table I. Some of these determinations were made on separate specimens from each side of the chest, others on specimens consisting

of a mixture of fluid from the two sides. Whenever the former was done, the difference between the two sides was negligible, so no distinction is made in Table I.

TABLE I

CHARACTERISTICS OF CHYLE

	DATE OBTAINED			
	FEB. 2, 1943	FEB. 16, 1943	MAR. 2, 1943	MAR. 10, 1943
Specific gravity				1.012
Total protein (Gm. %)	2.97			2.72
Albumin (Gm. %)	2.59			2.20
Globulin (Gm. %)	0.35			0.52
Nonprotein nitrogen (mg. %)	27.30			32.50
Total solids (Gm. %)		5.02		
Total fat (mg. %)		489.00	1,261	
Fatty acids (mg. %)			1,213	
Phospholipids (mg. %)			191	
Cholesterol (mg. %)			48	
Chlorides, as NaCl (mg. %)				620.00
Calcium (mg. %)				9.30
Inorganic phosphorus (mg. %)				6.20

The analyses on the fluid obtained on Feb. 16, 1943, were made by the Pevely Dairy Company of St. Louis, Mo. Those of March 2, 1943, were made by Dr. Augusta McCoord, of the Department of Pediatrics, University of Rochester School of Medicine, according to the methods of Bloor.[6, 7]

Absorption of Vitamin A and Beta Carotene.—Three tests were done. In the first, vitamin A was used, in the second, vitamin A and beta carotene together, and in the last beta carotene alone. The procedure in each was as follows: The baby was deprived of all supplemental sources of vitamin A for several days prior to each test, but was given formula as usual throughout the procedure. Both sides of the chest were emptied as completely as possible of fluid, and an initial blood sample obtained. Vitamin A and/or beta carotene were then administered orally, the former as a highly potent fish-liver oil, the latter in an oily solution. Blood and pleural fluid samples were then taken at given intervals for analysis. Because the analyses were carried out in two different laboratories in which different arbitrary units were

TABLE II

TIME	VITAMIN A			CAROTENE		
	BLOOD	LEFT CHEST	RIGHT CHEST	BLOOD	LEFT CHEST	RIGHT CHEST
Fasting	3.3	3.4		3.5	0.6	
3-hour specimen	10.0			6.0		
6½-hour specimen		34.4	12.4		1.2	0.0
7-hour specimen	4.9			4.5		
9½-hour specimen	3.4			3.0		

Test performed Feb. 25, 1943. Unfortunately, it was not possible to obtain fluid from the right pleural cavity just prior to the administration of the test material. Oleum percomorphum (Mead Johnson and Company) was used, the dose being 0.86 c.c. (47,000 units of vitamin A), figured on the basis of 0.1 c.c. of oil per pound of body weight. The analyses were made in the laboratories of the Department of Pediatrics, Washington University School of Medicine, by Dr. Harry Lawler, according to the method of May and associates,[8] and the values are expressed as arbitrary units of vitamin A and carotene per 100 c.c. of blood serum or chyle.

used to express the results, exact comparisons between the several tests are difficult. The results of these tests are shown in Tables II, III and IV.

TABLE III

TIME	VITAMIN A			CAROTENE			XANTHOPHYLL		
	BLOOD	BOTH SIDES MIXED		BLOOD	BOTH SIDES MIXED		BLOOD	BOTH SIDES MIXED	
Fasting	6.0	13.2		22	9		39	21	
		LEFT CHEST	RIGHT CHEST		LEFT CHEST	RIGHT CHEST		LEFT CHEST	RIGHT CHEST
5-hour specimen	34.4	282	79	14	26	17	39	21	21

Test performed on March 2, 1943. At this time 0.15 c.c. of a special fish-liver oil containing 210,000 units of vitamin A per cubic centimeter, together with 2 c.c. (15,000 units) of carotene in oil (S.M.A Corporation), was given. The samples of blood and chyle were collected under sterile conditions, and immediately sent to Dr. Augusta McCoord of Rochester, New York, who very kindly performed the analyses. Vitamin A analyses were done according to the method of Clausen and associates[9] and are expressed as Evelyn Photo-Electric units of vitamin A per 100 c.c. of blood serum or chyle, one E. P. U. being approximately equal to 3.8 I. U. of vitamin A. Those for carotene and xanthophyll were done by the method of Clausen and McCoord[10] and are expressed in gamma per 100 c.c.

In Tables II and III, it is seen that the concentration of vitamin A in the chyle rose rapidly following oral administration of the vitamin, but in neither test did the blood levels reach the values usually seen during vitamin A absorption tests. Moreover, the concentration of vitamin A rose to a significantly higher degree in the left chest as compared to the right. Carotene was absorbed poorly in one test (Table III) and not at all in the other (Table IV). Further, it should be noted that the oral administration of carotene did not influence the vitamin A content of the chyle (Table IV).

TABLE IV

TIME	VITAMIN A			CAROTENE		
	BLOOD	LEFT CHEST	RIGHT CHEST	BLOOD	LEFT CHEST	RIGHT CHEST
Fasting	1.7	0.0	0.6	2.3	0.0	0.9
4-hour specimen	4.2	0.0		5.4	2.0	
6½-hour specimen	3.5			2.3		
10½-hour specimen	3.5	2.2	2.1	3.5	2.0	2.0

Test performed on March 22, 1943. Two cubic centimeters (15,000 units) of carotene in oil (S.M.A. Corporation) were administered, no vitamin A being given. The baby was fasted for 8 hours preceding the test. The analytical methods were those used in the test of Feb. 25, 1943.

Vitamin D Absorption.—On April 2, 1943, the day of the baby's death, a vitamin D absorption test was carried out. After the usual preparation, 200,000 units of vitamin D were administered orally in the form of Ertron capsules,* and samples of blood and chyle were obtained at stated intervals. The specimens were then lyophilized, sealed in vacuo, and sent to Dr. Josef Warkany, who very kindly performed the biologic assays. Due to technical difficulties, not all of the analyses could be completed, but the following data are available. Whereas 2 c.c. of chyle taken in the fasting state were necessary to produce a two-plus healing in rachitic rats,[11] only 0.2 c.c. and 0.05 c.c. of chyle obtained four and

*Nutrition Research Laboratories, Chicago, Ill.

six hours, respectively, after administration of vitamin D were necessary to produce a like degree of healing. Thus the vitamin D content of the chyle had increased tenfold in four hours and fortyfold in six hours after administration of the vitamin D.

COMMENT

In contrast to the adult, in whom mechanical factors (tumors, traumatic rupture) are usually demonstrable, most of the reported cases of chylothorax in infants are of spontaneous origin. The cause is presumed to be either a congenital hypoplasia or defect in the thoracic duct. Defects have actually been demonstrated in some infants, but in general the pathologist finds it extremely difficult to dissect out accurately the thoracic lymph duct. It could not be found in the case here reported, nor was there evidence of lesions which could have produced obstruction to the duct. Any discussion as to the cause of the chylous effusion in this patient would thus be purely speculative.

The pathologic changes in the pancreas were quite striking, there being many regions in which insular tissue was so abundant as to occupy an entire high-power microscopic field. This hyperplasia was present in sections from three widely separated regions. The infant received many clyses of dextrose and of amigen, so the hyperplasia may have been the result of continually recurring hyperglycemia, as suggested previously by Hartmann and Jaudon.[12] The other postmortem observations were of doubtful significance. The changes noted in the adrenals and kidneys could hardly have contributed to the baby's death, and no clinical evidence of functional disturbance of these organs was noted. Serum calcium and phosphorus determinations were normal, as were repeated urinalyses.

If one remembers that chyle has certain definite characteristics, the diagnosis of chylothorax should not be difficult once fluid is obtained. The terms "pseudochylous" and "chyliform" are sometimes used to designate fluids which contain fat resulting from degeneration of leucocytes and the cells lining serous cavities. Chyle is the only form of finely emulsified fat present in the body fluids other than the blood, however, and consequently no other fluid can simulate its typical milky appearance. Many authors are in agreement with Gandin's[13] conclusions that chyle is unique. Confusion is not likely if one takes into account the high fat content (0.4 to 4.0 per cent), the absence of bacteria, and the characteristic gross appearance of the fluid.

The difficulties in demonstrating the duct at autopsy in small infants virtually obviate surgical repair during life. If obstructive lesions are present, surgery or irradiation might be of help; relief is often obtained through the establishment of collateral lymph channels. In the spontaneous variety, however, the only available treatment is that of repeated removal of fluid by thoracentesis. In the adult, apparent success has followed the use of phrenicotomy in a case of unilateral

chylothorax.[14] The injection of sterile broth into the pleural cavity has been tried in an effort to seal the leaking thoracic duct through formation of fibrous adhesions.[4]

Supportive therapy is of great importance, particularly in infants, as the continued withdrawal of relatively large amounts of fluid rich in fat and in protein is certain to impair the infant's nutritional status. The poor prognosis of chylothorax in infancy—four of the ten cases collected by Brescia[1] died—is directly related, as the case here reported illustrates, to the inanition which accompanies this condition. For this reason, parenteral food supplements in the form of plasma, amigen, and other fluids are definitely indicated. The readministration of the chyle intravenously seems to be a convenient and reasonably safe way of doing this, and reactions to this procedure were not observed in this patient.

The observations on the absorption of vitamin A and of beta carotene are in accord with those of Drummond, Bell, and Palmer.[3] Vitamin A was rapidly absorbed into the thoracic lymph from the gastrointestinal tract. While the fact that chylous fluid did not form as rapidly in the right pleural cavity as in the left may be related to the usual anatomic position of the thoracic duct, there is no obvious explanation for the difference between the two sides in the degree of rise in the vitamin A concentration during the absorption tests. Because fluid could not be obtained from the right pleural cavity prior to the first test, it was thought that the failure of the vitamin A content of the chyle to rise as rapidly on that side might possibly be due to the factor of dilution. However, the same result was obtained in the second test in which both pleural cavities were emptied as completely as possible at the start.

The blood level of vitamin A also rose following administration of the test material. The rise was much less than that usually seen in infants and children following a test dose of the vitamin, yet this patient absorbed enough vitamin A during life to remain free from clinical signs of vitamin A deficiency. Moreover, microscopic examination of the lungs and pancreas at autopsy revealed no evidence of epithelial metaplasia. In view of the lack of pathologic evidence of a complete obstruction to the thoracic duct in this patient, one can only conjecture as to the route vitamin A took in passing from the gastrointestinal tract into the blood. As suggested by Clausen,[2] direct absorption of the vitamin through the intestinal wall into the blood seems most likely, although it is impossible to exclude absorption from the pleural space.

The absorption of carotene was poor. The results shown in Table III indicate that this substance entered the chyle to a relatively small degree, while those of Table IV indicate a complete lack of absorption, for the range of values lies within the experimental error of the analytic method. This may have been due at least in part to the infection (bronchopneumonia) present at the time the latter test was performed.

Further, the infant was fasted prior to this test, which may have also retarded the absorption of the carotene. Both of these factors, infection, and the withholding of food, especially fat, are known to interfere with the absorption of carotene.[15]

To my knowledge, this is the first time that observations have been made on the absorption of vitamin D into the thoracic lymph. The data, though scanty, clearly indicate that the vitamin is fairly rapidly absorbed, the rate of absorption being roughly comparable to that of vitamin A.

SUMMARY

1. A case of spontaneous bilateral chylothorax in a 6-week-old infant is presented, together with a detailed analysis of the chyle. The patient succumbed, despite repeated thoracenteses and vigorous supportive therapy over a period of two months. Post-mortem examination failed to reveal a cause for the chylous effusion.

2. Absorption tests with vitamins A and D and beta carotene were performed. Vitamins A and D were rapidly absorbed into the chyle from the gastrointestinal tract and in appreciable quantities. Beta carotene was poorly absorbed.

3. Aspirated chyle was administered intravenously many times without untoward reactions.

4. The loss of protein through the repeated aspiration of chyle is fully as important as that of fat, if not more so. Supportive therapy in cases of chylothorax should include measures to maintain body protein stores.

REFERENCES

1. Brescia, M. A.: Arch. Pediat. **46:** 345, 1941.
2. Clausen, S. W.: The Harvey Lectures, 1942-43 edition, Lancaster, Pa., Science Press Printing Co., pp. 199-226.
3. Drummond, J. C., Bell, M. E., and Palmer, E. T.: Brit. M. J. **1:** 1208, 1935.
4. Schnug, E., and Ransohoff, J.: Surgery **41:** 278, 1943.
5. Whitcomb, B. B., and Scoville, W. B.: Arch. Surg. **45:** 747, 1942.
6. Bloor, W. R.: J. Biol. Chem. **24:** 227, 1916.
7. Bloor, W. R.: J. Biol. Chem. **77:** 53, 1928.
8. May, C. D., Blackfan, K. D., McCreary, J. F., and Allen, F. H.: Am. J. Dis. Child. **59:** 1167, 1940.
9. Clausen, S. W., Baum, W. S., McCoord, A. B., Rydeen, J. O., and Breese, B. B.: J. Nutrition **24:** 1, 1942.
10. Clausen, S. W., and McCoord, A. B.: J. Biol. Chem. **113:** 89, 1936.
11. Warkany, J., and Mabon, H. E.: Am. J. Dis. Child. **60:** 606, 1940.
12. Hartmann, A. F., and Jaudon, J. C.: J. PEDIAT. **11:** 1, 1937.
13. Gandin, S.: Ergebn. d. inn. Med. u. Kinderh. **12:** 218, 1913.
14. Nowak, S. J. G., and Barton, P. N.: J. Thoracic Surg. **10:** 628, 1941.
15. The Vitamins, Chicago, 1939, American Medical Association, pp. 33, 64.

CHYLOTHORAX IN A TWO-WEEK-OLD INFANT WITH SPONTANEOUS RECOVERY

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CHYLOTHORAX is a relatively rare condition which may occur at any age. Most cases are believed to result from rupture of the thoracic duct itself or of one of its tributaries. Among the various etiologic agents which have been observed are trauma, invasion by lymph node enlargement, thrombosis of the duct or of the vein into which it empties, and congenital weakness or abnormality of the duct system.

J. G., 2 weeks of age, was admitted to the Babies Hospital on July 23, 1943, with chief complaint of difficulty in breathing and blueness of the lips during the preceding twenty-four-hour period.

The infant was born at full term by normal, spontaneous delivery (weighing 3,460 Gm.), after the mother's first pregnancy. Both parents are healthy. There were no convulsions, cyanotic spells, or other abnormalities during his stay in the nursery. He was sent home in good condition at the age of 11 days (weighing 3,220 Gm.), breast fed, and receiving ascorbic acid and cod-liver oil in usual amounts.

Twenty-four hours before admission (age 13 days) his respirations were seen to be rapid and labored and his color was somewhat blue. These symptoms became progressively more intense until admission on the fourteenth day of life. There was no history of vomiting, trauma, convulsions, upper respiratory infection, or any known exposure to contagion.

Physical examination upon admission presented a desperately sick infant in acute respiratory distress. There was marked cyanosis of the entire body, and respirations were rapid and gasping. Auscultation of the chest revealed no audible breath sounds over the right lung field and scattered moist râles over the left lung field. The percussion note was flat on the right and dulled on the left. Marked shift of the heart border to the left was observed; the abdomen was moderately distended, and reflexes were physiologic.

Immediate fluoroscopy revealed a dense shadow filling the entire right hemithorax, with no aeration visible and marked shift of the mediastinum to the left. There was only a small portion of aerated lung visible in the left lower hemithorax.

Thoracentesis of the right pleural cavity was immediately performed by inserting a 20-gauge needle between the seventh and eighth ribs in the midscapular line posteriorly. Two hundred cubic centimeters of creamy yellowish fluid were obtained with ease. The infant withstood the procedure well, and immediate relief of respiratory embarrassment was observed. Examination shortly after thoracentesis presented a healthy appearing, hungry infant with a loud, vigorous cry. The temperature was 98.6° F.; pulse, 111; and respirations, 76. The lung fields were clear to percussion and auscultation. The heart rate was regular with point of maximum impulse in the sixth interspace in the left midclavicular line. The abdomen was moderately distended. The liver was 1 cm. below the costal margin. The spleen was not palpable. There was no lymphadenopathy.

From the Babies Hospital.

A tentative diagnosis of chylothorax was made, etiology unknown.

The laboratory data obtained soon after admission were as follows: Blood count: hemoglobin, 17.3 Gm. per 100 c.c. (120 per cent); red blood cells, 5,540,000 per cubic millimeter; leucocytes, 11,600 per cubic millimeter; polymorphonuclears, 75 per cent; lymphocytes, 15 per cent; monocytes, 10 per cent. Urine: pH 6.0;

TABLE I

CHEMICAL ANALYSIS OF CHYLOUS FLUID ASPIRATED FROM RIGHT PLEURAL CAVITY

	JULY 23 ON ADMISSION (PER 100 C.C.)	JULY 27 ON SKIMMED MILK DIET (PER 100 C.C.)	JULY 28 ON SKIMMED MILK DIET (PER 100 C.C.)	JULY 29 ON SKIMMED MILK DIET (PER 100 C.C.)	JULY 30 AFTER 12 HR. ON 4 PER CENT FAT FORMULA (PER 100 C.C.)
Nonprotein nitrogen	32.6 mg.				
Sugar	126.0 mg.				
Total protein	3.38 Gm.				
Phosphorus (as phosphate)	7.8 mg.	6.3 mg.			
Cholesterol	87.4 mg.	72.6 mg.			
Total lipid	1.81 Gm.	0.24 Gm.	0.056 Gm.	0.163 Gm.	1.44 Gm.

specific gravity, 1.018; albumin, very faint trace; sugar, 0; acetone, 0. Pleural fluid removed by thoracentesis: cell count, 18,675 per cubic millimeter; leucocytes, 16,700 per cubic millimeter, the majority of these being polymorphonuclears. Pleural fluid chemistry: see Table I. Nose and throat cultures: *Staphylococcus albus* hemolyticus (mannitol- and coagulase-positive), *Escherichia coli*, few beta hemolytic streptococci. Roentgenogram of the chest four hours after thoracentesis (Fig. 1):

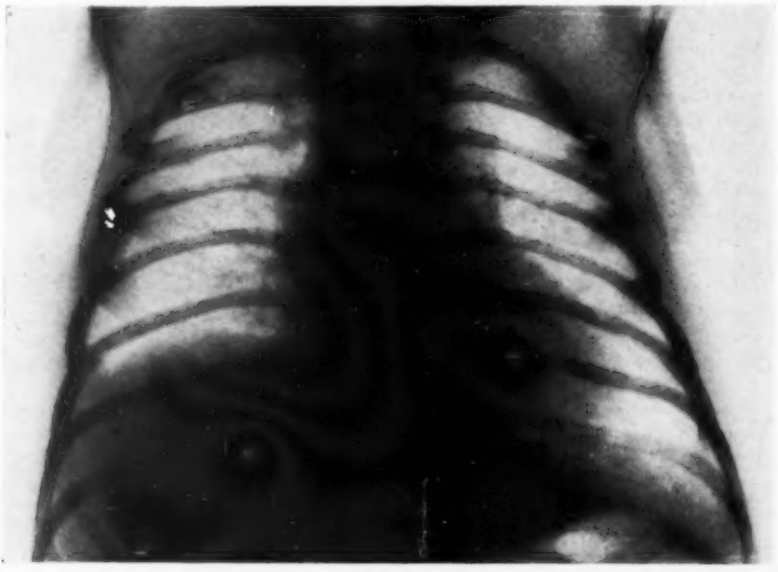

Fig. 1.—Day of admission, 4 hours after initial thoracentesis, 200 c.c. having been withdrawn; small amount of fluid in right pleural cavity; elevation of right diaphragm; slight shift of cardiac silhouette to left.

both lung fields clear; cardiac silhouette shifted slightly to left; evidence to suggest compression of the entire right lung field; small amount of pleural exudate present and a slight elevation of the right diaphragm. Impression: pleural effusion.

The infant was placed on sulfadiazine medication as a prophylactic measure against development of pneumonia. Eleven hours after admission, when re-examined, he showed no evidence of respiratory difficulty, and his lungs were clear to auscultation and percussion. Twenty-six hours after the first thoracentesis a moderate degree of respiratory distress was manifested by increased respiratory rate, and there were signs of fluid in the right lower lung field. Fluoroscopy suggested the presence of fluid in the right pleural cavity with shift of the mediastinum to the left.

A second thoracentesis was performed twenty-six hours after the first, yielding 55 c.c. of milky fluid, less creamy than on the preceding day. In the ensuing two weeks the respiratory rate rose on some occasions as high as 94 per minute without the accompaniment of cyanosis or other signs of embarrassment. Eventually respiratory distress would become apparent, associated with physical or fluoroscopic signs of pleural fluid. Thoracenteses were found to be necessary at approximately twenty-four-hour intervals during the first thirteen days of hospitalization, although on one occasion a forty-hour interval was allowed to occur, by which time respiratory distress had become quite marked. The volume of fluid aspirated is shown in Table II. On no occasion were any organisms cultivated from the aspirated fluid.

TABLE II

VOLUME OF FLUID ASPIRATED FROM THE RIGHT PLEURAL CAVITY

DAY OF ADMISSION	AGE (DAYS)	CHYLE REMOVED (C.C.)
1	14	200
2	15	55
3	16	63
5	18	130
6	19	110
7	20	130
8	21	105
9	22	95
10	23	90
11	24	120
12	25	120
13	26	60
Total		1,278

On the fourteenth hospital day there was no respiratory distress noted, and, although the breath sounds were slightly diminished over the right lower lung field and fluoroscopy showed a slight accumulation of fluid, thoracentesis was postponed in order to ascertain whether adequate absorption might take place without external drainage. No further thoracentesis was necessary after Aug. 4, 1943.

Subsequent roentgenograms of the chest revealed the following:

July 24, 1943 (second hospital day, just preceding thoracentesis; physical signs of fluid in right pleural cavity): All but a small portion of the central lower right lung field was obscured by fluid density. There was a marked shift of the mediastinal contents to the opposite (left) side. The left lung field was clear. The findings are those of pleural effusion.

Aug. 6, 1943 (fifteenth hospital day; Fig. 2): Large amount of air and pleural liquid visible in the right pleural space. This is interpreted as being due to air having been sucked in during repeated aspirations, although the possibility of laceration of the lung cannot be ruled out.

Aug. 13, 1943 (twenty-second hospital day): Only a small amount of air and pleural liquid were visible.

Aug. 20, 1943 (twenty-ninth hospital day): There was no evidence of air. A dense shadow noted in the diaphragmatic segment of the right pleural space was interpreted as fluid.

Fig. 2.—Fifteenth hospital day. Air and fluid in right pleural cavity.

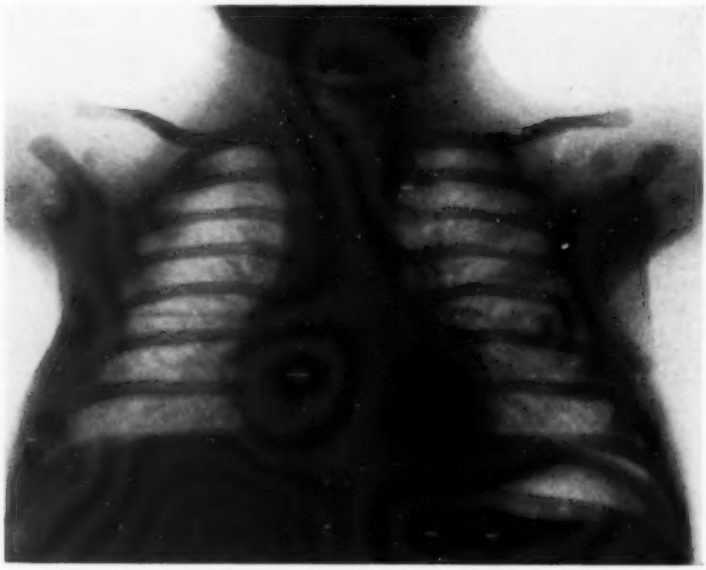

Fig. 3.—Thirty-sixth hospital day. A linear shadow outlined the lesser interlobar fissure in the right lung. Chylothorax had disappeared.

Aug. 27, 1943 (thirty-sixth hospital day; Fig. 3): There were fine linear shadows of increased density in the interlobar fissures of the right lung; otherwise no abnormality. Chylothorax had disappeared completely.

Sept. 8, 1943 (forty-eighth hospital day): No pathologic changes were visible.

During the first two weeks of the infant's hospital course he was fed for the most part on a skimmed milk formula, enriched at first with 10 per cent cane sugar, later by the addition of powdered casein. Beginning on the seventh hospital day, he was given an evaporated milk formula for a twenty-four-hour period, but this was discontinued because of the appearance of mild diarrhea. There was no evidence that the two events were related, but the infant had been progressing well on the skimmed milk formula and it seemed logical to maintain a low fat intake in an attempt to lessen the flow through the thoracic channels.

A vitamin A absorption test* was carried out on the seventh hospital day. The results, given in Table III, show a delay in absorption, the peak level occurring at twenty-four hours in place of the customary four to six hours. The presence of vitamin A in the chylous fluid, both in the fasting sample and in the twenty-four-hour sample, is of interest.

TABLE III

VITAMIN A ABSORPTION TEST IN INFANT WITH CHYLOTHORAX (RESPONSE TO ORAL ADMINISTRATION OF 7,000 UNITS PER KILOGRAM OF BODY WEIGHT, GIVEN AS OLEUM PERCOMORPHUM)

	VITAMIN A CONCENTRATION IN INTERNATIONAL UNITS PER 100 C.C.	
	BLOOD SERUM	PLEURAL FLUID
Fasting	100	150
8 hours	215	
24 hours	332	Over 400

On the fourteenth hospital day, twenty-four hours after the final thoracentesis, a watery diarrhea commenced; this lasted for a two-week period and resulted in several episodes of dehydration, acidosis, and edema associated with hypoproteinemia. Supportive therapy consisting of hypodermoclyses and intravenous administration of glucose-saline solutions and plasma was carried out as needed. At no time during the diarrheal episodes were any pathogens found on stool culture, nor was there any marked leucocytosis, although the proportion of eosinophiles reached 10 per cent. Sulfadiazine was maintained by mouth during this time.

Thirteen days after the onset of diarrhea the right eardrum was observed to be somewhat dull, and myringotomy was performed, yielding a small amount of serous fluid, culture of which revealed *Staphylococcus aureus* hemolyticus (mannitol- and coagulase-positive). At the same time the blood sulfadiazine level was found to be less than 3 mg. per 100 c.c., and medication by subcutaneous route was started (5 per cent sodium sulfadiazine in distilled water given in the usual 0.1 Gm. per kilogram of body weight dosage) in an attempt to maintain a higher blood level. A diagnostic thoracentesis was carried out at this time, and only a few cubic centimeters of clear fluid were obtained, culture of which proved sterile. The presence of a persistent eosinophilia raised the question as to whether the diarrhea might be on an allergic basis, and in view of this the formula was changed from one of milk protein base to one of soybean base. Within thirty-six hours after the three events took place (namely, myringotomy, increasing of the sulfadiazine level, and change of formula) the diarrhea ceased. There was no noticeable reduction in eosinophilia while the patient took the soybean preparation, and return

*Vitamin A in the form of oleum percomorphum and at a dosage of 7,000 units per kilogram of body weight was fed and blood levels of vitamin A determined at 0, 8, and 24 hours.

to cow's milk formula a few days later did not cause exacerbation of the diarrhea. At no time during the patient's hospital stay did he have fever. His right ear continued to drain moderately for the ensuing eight days, and sulfadiazine was maintained for one week after cessation of drainage.

When the infant left the hospital, seven weeks after admission, he exhibited no clinical or roentgenographic signs of illness. He was sent home on a half-skimmed milk formula (2 per cent fat) and has been followed since discharge in the outpatient clinic. When last seen, Feb. 4, 1944, he was in excellent condition.

REVIEW OF THE LITERATURE

In this case of chylothorax, as in several other reported instances, the etiology and pathology remain unknown. Considerable variation has been observed in the anatomy of the thoracic duct, but it usually lies parallel to the vertebral column, just to the right of the lateral margin of the vertebral bodies, and joins the venous system at the junction of the left internal jugular and left subclavian veins. All lymphatics below the diaphragm are believed to drain through this channel. Brescia[1] has described the presence of a valve at the cephalic end of the duct which prevents backflow of blood into the lymphatic system. The rate of flow of chyle is not constant, but is increased after feedings and also by vigorous respiratory activity.

Little, Harrison, and Blalock[2] have described experimental work in dogs, in which the thoracic duct was tied off without the production of chylothorax or of any other abnormality. Occluding the subclavian vein, however, did result in the appearance of chylothorax, presumably from rupture of the duct, in one-half of the animals. Andersen[3] found that tying off the duct in cats resulted in no effusion of chyle, nor any other noticeable abnormality.

Sherman[4] in 1907 reported a case of chylothorax in a four-and-one-half-year-old boy who four months previously had fallen down a flight of stairs. Three aspirations were performed within two weeks, and the child recovered spontaneously. Sherman also discussed eleven published cases, all in patients under 14 years of age, five of which were connected with trauma, at least chronologically, and the remainder with an infectious process, usually of a type associated with mediastinal lymphadenopathy.

Jennings and Rich[5] reported a case in 1908 occurring in a 9-month-old infant who had had a preceding upper respiratory infection six weeks before. Aspirations were carried out as needed to relieve respiratory difficulty at intervals varying from two to four weeks, over an eleven-month period. A total of over eleven liters of fluid was withdrawn, after which time spontaneous recovery occurred.

Lewin[6] in 1916 reported a case in an adult associated with leucemic infiltration of the mediastinal nodes. Brescia[1] discussed the anatomy involved and reported a case in a 13-month-old child which began after

a two-week episode of pneumonia associated with a hacking cough. Aspirations were carried out three times within ten days and the infant recovered.

Pisek[7] in 1917 reported a case in a 9-week-old infant who ten days before had suffered an attack of convulsions and hyperpnea. After two aspirations the infant recovered spontaneously. Stewart and Linner[8] in 1926 described a case in a 4-day-old infant who died on the twentieth day of life, after numerous aspirations. Autopsy revealed displacement of the mediastinum to the left and presence of chylous fluid in the right pleural sac with atelectasis of the right lung. Attempt to locate the thoracic duct was unsuccessful. There was no history of trauma, convulsion, or infection in this case.

Heppner[9] in 1934 cited an example in an adult who had been in an automobile accident and who subsequently displayed signs of chylothorax several weeks after the injury. In view of the fact that repeated thoracenteses, carried out over several weeks' time, afforded only temporary relief, operative intervention was undertaken: the thoracic duct was approached and ligated through a ventral incision parallel to the vertebrae at the tenth thoracic level, and a drain was inserted. The patient withstood the operative procedure and immediate postoperative period well only to die suddenly twenty-four hours later. Autopsy revealed massive bilateral adrenal hemorrhage as well as interruption in the continuity of the thoracic duct and fibrosis of its distal end.

Yater[10] in 1935 reported a case in a 47-year-old woman due to carcinomatous involvement of the mediastinal lymph nodes. Bauersfeld[11] observed an instance of chylothorax in an adult who had been in an automobile accident and who recovered after several thoracenteses.

Everhart and Jacobs[12] have reviewed the clinical literature and list sixty-nine cases of chylothorax, five of which occurred in children under 1 year of age. They have also included a case of their own in a 15-day-old infant which terminated fatally on the thirty-sixth day of life, after frequent aspirations. Autopsy revealed the presence of chylous fluid in the right thoracic cavity, and a leakage point adjacent to the mediastinum was disclosed when pressure was applied to the abdomen. The thoracic duct was not identified.

Little; Harrison, and Blalock[2] reported in detail the case of a 17-year-old girl who ten weeks before admission to hospital had been in an automobile accident. Shortly before admission she developed respiratory difficulty associated with a moderate amount of pain in the chest. Chylous fluid was found in the left pleural cavity and in the peritoneal cavity. The patient was placed on a fat-free diet, and aspirations were carried out as often as necessary to relieve respiratory embarrassment. After twelve weeks without noticeable improvement other than tem-

porary relief at the time of aspiration, an exploratory operation was performed through an incision in the left supraclavicular region. Near the junction of the internal jugular and subclavian veins several large lymph vessels containing chyle were found, as well as some enlarged nodes. A number of the smaller blood vessels were thrombosed, and the internal jugular vein was occluded by a thrombus. The incision was closed without drainage. There were no postoperative complications other than numbness and edema of the legs; however, repeated aspirations were still needed at the time the report was published, eighteen months after the onset of the illness. Reinjection of the aspirated chyle into veins of the arm was performed for a three-month period after the operation but was discontinued for lack of noticeable improvement. The possibility that chylous fluid might favor venous thrombosis was entertained. Detailed chemical studies were carried out, and it was observed that the accumulation of chyle in the body cavities could be decreased if the patient was maintained on a fat-free diet. Considerable stress was placed upon the protein loss in chylous fluid, since the patient exhibited hypoproteinemia, marked generalized edema, and malnutrition.

Peet and Campbell[13] reported a case occurring ten days after the performance of a supradiaphragmatic splanchnicectomy in an adult patient. Operative intervention was attempted after two weeks of repeated aspiration; the duct was freed and ligated, but a few minutes later the patient suddenly expired.

This brief review of the literature indicates that there is little unanimity as to treatment and also little success in the reported efforts at surgical repair. The necessity of repeated aspiration and of adequate dietary control seems obvious.

DISCUSSION

This case of chylothorax in a 14-day-old infant is of interest because of its rarity and also because of the spontaneous recovery.

Repeated questioning of the parents of the infant failed to disclose any history of trauma or convulsive episode prior to the onset of the condition. At no time during the early part of the hospital stay was there any evidence of infection. The sudden appearance of a watery diarrhea, coinciding with a diminishing accumulation of pleural fluid, was never satisfactorily explained. The existence of a low-grade infection in the pleural cavity, as the basis of both the diarrhea and the sealing off of the source of the fluid, was postulated but received no support from bacteriologic studies.

Surgical intervention was considered several times during the early period of hospitalization. However, the difficulty of the surgical approach, the uncertainty of accomplishing a satisfactory repair of the

duct, and the infant's excellent general condition combined to counsel postponement until it became clear that the patient had solved his own problem.

The decision to maintain the infant on a low fat and high protein diet was largely motivated by the work of Little, Harrison and Blalock.[2] These investigators demonstrated that the rate of fluid accumulation in their patient was directly proportional to the dietary fat intake, and they also observed a tremendous protein loss through aspiration of chyle. Our infant was losing approximately 5 Gm. of protein daily in the discarded aspirate, and, in order to counteract this, 10 Gm. of extra protein were added to the skimmed milk formula in the form of Casec.*

The matter of intravenous reinjection of the aspirated chylous fluid was considered, as well as feeding by mouth, but no adequate reason could be found to justify either procedure. Little and his colleagues, in their case, did reinject the fluid over a three-month period but discontinued it on the grounds that no beneficial effects were noted. Since our patient's dietary intake seemed adequate in protein, minerals, vitamins, and total energy, no indication for the added ingestion of chyle was apparent. In fact, an exceptionally high caloric intake of 160 to 200 calories per kilogram was maintained in order to make up for the loss in the daily aspirations.

The alteration of the fat content and the general appearance of the aspirated fluid from time to time is worthy of note. The first sample, taken from the admission aspiration and preceding which time the infant had been fed on breast milk, was creamy yellow in appearance and contained 1.81 per cent fat. Succeeding samples, while the infant was on a skimmed milk formula with less than 0.5 per cent fat, were somewhat watery in appearance and contained on the fifth day 0.24 per cent fat, on the sixth day, 0.056 per cent fat, and on the seventh day, 0.163 per cent fat. On the seventh hospital day, after the aspiration was carried out, the feeding was changed to an evaporated milk formula containing 4 per cent fat. Aspiration on the following day yielded 105 c.c. of creamy material which contained 1.44 per cent fat. We did not find, as we expected to, and as Little and his colleagues did, an increase in the amount of fluid produced along with the higher fat intake. However, we had the benefit of only a single observation; with the onset of diarrhea the formula was shifted back to skimmed milk and no further studies of this question were possible.

It is interesting to note that the amount of fat recovered from the pleural cavity was somewhat less than 10 per cent of the dietary intake of fat, at both high and low levels of fat consumption. On the skimmed milk diet the fat fed was about 3 Gm. a day, and the quantity withdrawn by aspiration was 0.2 Gm. On the evaporated milk diet the intake was 21 Gm., the amount aspirated being 1.52 Gm. No attempt was

*Mead Johnson & Co., Evansville, Ind.

made to be certain that all the fluid was aspirated. However, all that could be easily removed was obtained at each aspiration, and fluoroscopy after thoracenteses confirmed the expansion of the lung. We interpreted this discrepancy in fat intake and chylous fat loss to mean that only a part of the absorbed fat, and probably also only part of the chylous fluid delivered into the thoracic duct, was escaping into the pleural cavity. This phenomenon could result from leakage in a small tributary rather than from rupture of the duct itself, if one assumes that branches of the mesenteric lymphatics may at times join the thoracic duct above the diaphragm.

Several further studies were contemplated, such as the relationship between fat ingestion and fat elimination in stools and the effect of varying protein and carbohydrate intake on the chemical composition of the chylous fluid, but the patient's recovery removed the opportunity for carrying out these plans.

SUMMARY

A case of chylothorax in a 14-day-old infant is presented. The patient recovered following repeated aspiration of the right pleural cavity, over a period of about two weeks, for relief of recurrent respiratory difficulty.

A brief review of the literature dealing with chylothorax is given, and a few observations dealing with the nature of the chylous fluid in relation to dietary intake are cited.

REFERENCES

1. Brescia, M. A.: Arch. Pediat. **58**: 345, 1941.
2. Little, J. M., Harrison, C., and Blalock, A.: Surgery **11**: 392, 1942.
3. Andersen, D. H.: Personal communication, unpublished observations.
4. Sherman, De W. H.: Arch. Pediat. **24**: 646, 1907.
5. Jennings, Ç. G., and Rich, H. M.: Arch. Pediat. **25**: 195, 1908.
6. Lewin, P.: Am. J. M. Sc. **152**: 71, 1916.
7. Pisek, G. R.: Arch. Pediat. **34**: 929, 1917.
8. Stewart, C. A., and Linner, H. P.: Am. J. Dis. Child. **31**: 654, 1926.
9. Heppner, G. J.: J. A. M. A. **102**: 1294, 1934.
10. Yater, W. M.: Ann. Int. Med. **9**: 600, 1935.
11. Bauersfeld, E. H.: J. A. M. A. **109**: 16, 1937.
12. Everhart, J. K., and Jacobs, A. H.: J. PEDIAT. **15**: 558, 1939.
13. Peet, M. M., and Campbell, K. N.: Univ. Hosp. Bull., Ann. Arbor **9**: 2, 1943.

EARLY INFANTILE AUTISM

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DURING the past six years, I have become increasingly interested in a number of children, twenty by now, whose behavior differs uniquely and markedly from anything reported so far. Among the individual patients there are great variations in the degree of the disturbance, in the manifestation of specific features, and in the step-by-step development in the course of time. Yet in spite of this seeming divergence they all present essential common characteristics to such an extent that they cannot but be considered as fundamentally alike from the point of view of psychopathology. Many of these children were brought to us primarily with the assumption that they were severely feeble-minded or with the question of auditory impairment. Psychometric test performances yielded indeed very low quotients, and often enough absent or inadequate responses to sounds of any kind gave good reason for the suspicion of deafness. But careful examination showed very soon that the children's cognitive potentialities were only masked by the basic affective disorder; in fact, a few of the children had started out by amazing their parents with phenomenal feats of rote repetition. In all instances it could be established that hearing as such was not defective.

The common denominator in all these patients is their disability to relate themselves in the ordinary way to people and situations from the beginning of life. Their parents referred to them as always having been "self-sufficient," "like in a shell," "happiest when left alone," "acting as if people weren't there," "giving the impression of silent wisdom." The case histories indicate invariably the presence from the start of *extreme autistic aloneness* which, wherever possible, disregards, ignores, shuts out anything that comes to the child from the outside. Almost every mother recalled her astonishment at the child's failure to assume at any time the usual anticipatory posture preparatory to being picked up. According to Gesell this kind of adjustment occurs universally at 4 months of age.

Two case histories may serve to illustrate the principal features:

CASE 1.—Paul G. was referred in March, 1941, at the age of 5 years for psychometric assessment of what was thought to be a severe intellectual defect. He had attended a nursery school where his incoherent speech, inability to conform, and temper outbursts created the impression of feeble-mindedness.

Paul, an only child, when nearly 2 years of age, had come to this country from England with his mother. The father, a mining engineer, had left his wife after several years of an unhappy marriage. The mother, a restless, unstable, excitable woman, gave a vague and blatantly conflicting history of the family background

and the child's development. She spent much time emphasizing and illustrating her efforts to make Paul clever by teaching him to memorize poems and songs. At 3 years, he knew the words of not less than 37 songs and various and sundry nursery rhymes.

He was born normally. He vomited a great deal during his first year and feeding formulas were changed frequently with little success. He cut his teeth, held up his head, sat up, walked, and established bowel and bladder control at the usual age. He had measles, chicken pox, and pertussis without complications. On physical examination, phimosis was found to be the only deviation from otherwise good health.

Paul was a slender, well-built, attractive child, whose face looked intelligent and animated. He had good manual dexterity. He rarely responded to any form of address, even to the calling of his name. At one time he picked up a block from the floor on request. Once he copied a circle immediately after it had been drawn before him. Sometimes an energetic "Don't!" caused him to interrupt his activity of the moment. But usually, when spoken to, he went on with whatever he was doing as if nothing had been said. Yet one never had the feeling that he was willingly disobedient or contrary. He was obviously so remote that the remarks did not reach him. He was always vivaciously occupied with something and seemed to be highly satisfied unless someone made a persistent attempt to interfere with his self-chosen actions. Then he first tried impatiently to get out of the way and, when this met with no success, screamed and kicked in a full-fledged tantrum.

There was a marked contrast between his relations to people and to objects. Upon entering the room he instantly went after objects and used them correctly. He was not destructive and treated the objects with care and even affection. He picked up a pencil and scribbled on paper that he found on the table. He opened a box, took out a toy telephone, singing again and again: "He wants the telephone," and went around the room with the mouthpiece and receiver in proper position. He got hold of a pair of scissors and patiently and skilfully cut a sheet of paper into small bits, singing the phrase, "Cutting paper," many times. He helped himself to a toy engine and ran around the room holding it up high and singing over and over again, "The engine is flying." While these utterances, made always with the same inflection, were clearly connected with his actions, he ejaculated others that could not be linked up with immediate situations. These are a few examples: "The people in the hotel," "Did you hurt your leg?" "Candy is all gone, candy is empty," "You'll fall off the bicycle and bump your head." However, some of those exclamations could be definitely traced to previous experiences. He was in the habit of saying almost every day, "Don't throw the dog off the balcony." His mother recalled that she had said those words to him about a toy dog while they were still in England.

None of these remarks was meant to have communicative value. He behaved as if people, as such, did not matter or even exist. It made no difference whether one spoke to him in a friendly or a harsh way. He never looked up at people's faces. When he had any dealings with persons at all, he treated them, or rather parts of them, as if they were objects. He would use a hand to lead him. He would, in playing, butt his head against his mother as at other times he did against a pillow. He allowed his boarding mother's hands to dress him, paying not the slightest attention to *her*. When with other children he ignored them and went after their toys.

His enunciation was clear and he had a good vocabulary. His sentence construction was satisfactory with one significant exception. He never used the pronoun of the first person, nor did he refer to himself as Paul. All statements pertaining to himself were made in the second person, as literal repetitions of things that had been said to him before. He would express his desire for candy

by saying, "*You* want candy." He would pull his hand away from a hot radiator and say, "*You* get hurt."

Formal testing could not be carried out, but he certainly could not be regarded as feeble-minded in the ordinary sense. After hearing his boarding mother say grace three times, he repeated it without a flaw and has retained it since then. He could count and name colors. He learned quickly to identify his favorite victrola records from a large stack and knew how to mount and play them.

His boarding mother reported a number of observations that indicated compulsive behavior. He often masturbated with complete abandon. He ran around in circles emitting phrases in an ecstatic-like fashion. He could continue in this manner for a long time and showed great irritation when he was interfered with. All these and many other things were not only repetitions but recurred day after day with almost photographic sameness.

CASE 2.—Charles N. was brought by his mother on February 2, 1943, at 4 years of age, with the chief complaint, "The thing that upsets me most is that I can't reach my baby."

As a baby the boy had been inactive, "slow and phlegmatic." He would lie in the crib, just staring. He would act almost as if hypnotized. He seemed to concentrate on doing one thing at a time. Hypothyroidism was suspected, and he was given thyroid extract, without any change of the general condition.

His mother reported: "When he was 1½ years old, he could discriminate between 18 symphonies. He recognized the composer as soon as the first movement started. He would say, 'Beethoven.' At about the same age, he began to spin toys and lids of bottles and jars by the hour. He had a lot of manual dexterity in ability to spin cylinders. He would watch them and get severely excited and jump up and down in ecstasy. Now he is interested in reflecting light from mirrors and catching reflections. When he is interested in a thing, you cannot change it. He would pay no attention to me and show no recognition of me if I entered the room.

"The most impressive thing is his detachment and his inaccessibility. He walks as if he is in a shadow, lives in a world of his own where he cannot be reached. No sense of relationship to persons. He went through a period of quoting another person; he never offers anything himself. His entire conversation is a replica of whatever has been said to him. He used to speak of himself in the second person; now he uses the third person at times.

"He is destructive; the furniture in his room looks like it has hunks out of it. He will break a purple crayon into two parts and say, '*You* had a beautiful purple crayon and now it's two pieces. Look what *you* did.'

"When he is with other people, he doesn't look up at them. Last July we had a group of people. When Charles came in, he was just like a foal who had been let out of an enclosure. He did not pay attention to them but their presence was felt. He will mimic a voice and he sings and some people would not notice any abnormality in the child. At school he never envelops himself in a group; he is detached from the rest of the children except when he is in the assembly; if there is music, he will go to the front row and sing.

"He has a wonderful memory for words. Vocabulary is good, except for pronouns. He never initiates conversation and his conversation is limited; it is extensive only as far as objects go."

Charles was born normally, a planned and wanted child. He sat up at 6 months of age and walked at less than 15 months. "He just stood up and walked one day, no preliminary creeping." He has had none of the usual children's diseases.

Charles is the oldest of three children. The father, a high school graduate and a clothing merchant, is described as a "self-made, gentle, calm, and placid person." The mother has "a successful business record, a theatrical booking office

in New York; she is of remarkable equanimity." The other two children were 28 and 14 months old at the time of Charles's visit to the Clinic. The maternal grandmother, "very dynamic, forceful, hyperactive, almost hypomanic," has done some writing and composing. A maternal aunt, "psychoneurotic, very brilliant, given to hysterics," has written poems and songs. Another aunt was referred to as "the amazon of the family." A maternal uncle, a psychiatrist, has considerable musical talent. The paternal relatives were described as "ordinary simple people."

Charles was a well-developed, intelligent-looking boy, who was in good physical health. He wore glasses. When he entered the office, he paid not the slightest attention to the people present (three physicians, his mother, and his uncle). Without looking at anyone, he said, "Give me a pencil!" Then he took a piece of paper from the desk and wrote something resembling a figure two (a large desk calendar prominently displayed a figure 2; the day was February 2). He had brought with him a copy of *Reader's Digest* and was fascinated by a picture of a baby. He said, "Look at the funny baby," innumerable times, occasionally adding, "Is he not funny? Is he not sweet?"

When the book was taken away from him, he struggled with the hand that held it, without looking at the *person* who had taken the book. When he was pricked with a pin, he said, "What's this?" and answered his own question: "It is a needle." He looked timidly at the pin, shrank from further pricks, but at no time did he seem to connect the pricking with the *person* who held the pin. When the *Reader's Digest* was taken from him and thrown on the floor and a foot placed over it, he tried to remove the foot as if it were another detached and interfering object, again with no concern for the *person* to whom the foot belonged. He once turned to his mother and excitedly said, "Give it to *you!*"

When confronted with the Seguin form board, he was mainly interested in the names of the forms, before putting them into their appropriate holes. He often spun the forms around, jumping up and down excitedly while they were in motion. The whole performance was very repetitious. He rarely used language as a means of communicating with people. He remembered names, such as "octagon," "diamond," "oblong block," but nevertheless kept asking, "What is this?"

He did not respond to being called and did not look at his mother when she spoke to him. When the blocks were removed, he screamed, stamped his feet, and cried, "I'll give it to you!" (meaning, "You give it to me"). He was very skilful in his movements.

In spite of great individual differences, the twenty children* of the group (sixteen boys and four girls) presented the same basic features of extreme autistic aloneness. Thirteen children acquired the ability to speak, while seven have remained mute so far. But language, even when present, did not, over a period of years, serve to convey meaning to others. Naming presented no difficulty; even long and unusual words were retained with remarkable facility. An excellent rote memory, retaining many poems, songs, lists of presidents, and the like, made the parents at first think of the children proudly as child prodigies.

As far as the communicative functions of speech are concerned, there is no essential difference between the speaking and the mute children. Even some of the "mute" children were reliably reported to have surprised the observers on occasions by uttering single words. One clearly

*Eleven of the twenty cases have been reported by me in the Nervous Child 2: 217, 1943.

once said, "good night," another said, "overalls," and one said, "mama," "baby," "chocolate," and "marshmallow."

When sentences are finally formed, they are for a long time mostly parrotlike repetitions of heard word combinations. They are sometimes echoed immediately, but they are just as often "stored" by the child and uttered at a later date. One may, if one wishes, speak of *delayed echolalia*. Affirmation is indicated by literal repetition of a question. "Yes" is a concept that it takes the children many years to acquire. They are incapable of using it as a general symbol of assent. One child learned to say "yes" when his father told him that he would put him on his shoulders if he said "yes." This word then came to "mean" only the desire to be put on his father's shoulders. It took many months before he could detach the word "yes" from this specific situation, and it took much longer before he was able to use it as a general term of affirmation.

The same type of *literalness* exists also with regard to prepositions. Alfred, when asked, "What is this picture about?" replied: "People are moving *about*."

John F. corrected his father's statement about pictures on the wall; the pictures were "*near* the wall." Donald T., requested to put something *down*, promptly put it on the floor. Apparently the meaning of a word becomes inflexible and cannot be used with any but the originally acquired connotation.

There is no difficulty with plurals and tenses. But the absence of spontaneous sentence formation and the echolalia type reproduction has, in every one of the speaking children, given rise to a peculiar grammatical phenomenon. *Personal pronouns are repeated just as heard*, with no change to suit the altered situation. The child, once told by his mother, "Now I will give you your milk," expresses the desire for milk in exactly the same words. Consequently, he comes to speak of himself always as "you," and of the person addressed as "I." Not only the words, but even the intonation is retained. If the mother's original remark has been made in the form of a question, it is reproduced with the grammatical form and the inflection of a question. The pronominal fixation remains until about the sixth year of life, when the child gradually learns to speak of himself in the first person, and of the individual addressed in the second person. In the transitional period, he sometimes still reverts to the earlier form or at times refers to himself in the third person.

The child's behavior is governed by an *anxiously obsessive desire for the maintenance of sameness* that nobody but the child himself may disrupt on rare occasions. Changes of routine, of furniture arrangement, of a pattern, of the order in which everyday acts are carried out can drive him to despair. When John's parents were ready to move to a new home, the child was frantic when he saw the moving men roll up the rug in his room. He was acutely upset until the moment when in

the new home he saw his furniture arranged in the same manner as before. He looked pleased, all anxiety was suddenly gone, and he went around affectionately patting each piece. Once blocks, beads, sticks have been put together in a certain way, they are always regrouped in exactly the same way, even though there was no definite design. The children's memory was phenomenal in this respect. After the lapse of several days a multitude of blocks could be rearranged in precisely the same unorganized pattern, with the same color of each block turned up, with each picture or letter on the upper surface of each block facing in the same direction as before. The absence of a block or the presence of a supernumerary block was noticed immediately, and there was an imperative demand for the restoration of the missing piece. If someone removed a block, the child would struggle to get it back, going into a panic tantrum until he regained it, and then promptly and with sudden calm after the storm would return to the design and replace the block.

Every one of the twenty children has a good relation to objects; he is interested in them; he can play with them happily for hours. He can be very fond of them, or get angry at them if, for instance, he cannot fit them into a certain space. When with them he has a gratifying sense of undisputed power and control. Donald and Charles began in the second year of life to exercise this power by spinning everything that possibly could be spun and jumping up and down in ecstasy when they watched the objects whirl about. Frederick "jumped up and down in great glee" when he bowled and saw the pins go down. The children sensed and exercised the same power over their own bodies by rolling and other rhythmic movements. These actions and the accompanying ecstatic fervor strongly indicate the presence of *masturbatory gratification.*

The children's *relation to people* is altogether different. Every one of the children upon entering the office immediately went after blocks, toys, or other objects without paying the least attention to the persons present. It would be wrong to say that they were not aware of the presence of persons. But the people, as long as they left the child alone, figured in about the same manner as did the desk, the bookshelf, or the filing cabinet. When the child was addressed, he was not bothered. He had the choice between not responding at all or, if a question was repeated too insistently, "getting it over with" and continuing with whatever he had been doing. Comings and goings, even of the mother, did not seem to register. Conversation going on in the room elicited no interest. If the adults did not try to enter the child's domain, he would at times while moving between them gently touch a hand or a knee as on other occasions he patted the desk or the couch. But he never looked into anyone's face. If an adult forcibly intruded himself by taking a block away or stepping on an object that the child needed, the child struggled and became angry

with the hand or the foot, which was dealt with per se and not as a part of a person. He never addressed a word or a look to the owner of the hand or foot. When the object was retrieved, the child's mood changed abruptly to one of placidity. When pricked he showed fear of the *pin* but not of the person who pricked him.

Even though most of these children were at one time or another looked upon as feeble-minded, they are all unquestionably endowed with good *cognitive potentialities*. They all have strikingly intelligent physiognomies. Their faces at the same time give the impression of *serious-mindedness* and, in the presence of others, an anxious *tenseness*, probably because of the uneasy anticipation of possible interference. When alone with objects there is often a placid smile and an expression of beatitude sometimes accompanied by happy though monotonous humming and singing. The astounding vocabulary of the speaking children, the excellent memory for events of several years before, the phenomenal rote memory for poems and names, and the precise recollection of complex patterns and sequences, bespeak good intelligence in the sense in which this word is commonly used. Binet or similar testing could not be carried out because of limited accessibility. But all the children did well with the Seguin form board.

There is one other very interesting common denominator in the backgrounds of these children. Among the parents, grandparents, and collaterals there are many physicians, scientists, writers, journalists, and students of art. Nine of the twenty families are represented either in *Who's Who in America* or in *American Men of Science*, or in both.

It is not easy to evaluate the fact that all of our patients have come of highly intelligent parents. This much is certain, that there is a great deal of obsessiveness in the family background. The very detailed diaries and reports and the frequent remembrance, after several years, that the children had learned to recite 25 questions and answers of the Presbyterian Catechism, to sing 37 nursery songs, or to discriminate between 18 symphonies, furnish a telling illustration of parental obsessiveness.

One other fact stands out prominently. In the whole group there are very few really warmhearted fathers and mothers. For the most part the parents, grandparents, and collaterals are persons strongly preoccupied with abstractions of a scientific, literary, or artistic nature and are limited in genuine interest in people. Even some of the happiest marriages are rather cold and formal affairs. The question arises whether or to what extent this fact has contributed to the condition of the children. The children's aloneness from the beginning of life makes it difficult to attribute the whole picture exclusively to the type of the early parental relations with our patients.

MYASTHENIA GRAVIS—ITS OCCURRENCE IN A SEVEN-YEAR-OLD FEMALE CHILD

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MYASTHENIA gravis is a disease which manifests itself by excessive fatigability of the musculature. While it is not common, there appears to have been a notable increase in its frequency since the epidemic of epidemic encephalitis which centered around 1920. It is a condition likely to show remissions almost as conspicuously as multiple sclerosis.

Myasthenia gravis begins in early life and usually in the third decade. Grinker[1] in his textbook remarks that individuals as young as 15 years of age have been affected, but his statement requires modification as a small series of reported cases shows that it can occur in much younger children.

The first case in a child was described by Remak[2] in a girl 12 years of age. Gerstle[3] in 1929 reviewed the age incidence of the disease and noted two cases under the age of 10, and twelve cases before the age of 20. In a detailed study of eighty-seven cases, covering a period of sixteen years, Kennedy and Moersch[4] reported the following age distribution: twenty-seven began in the third decade; eighteen, in the fourth; thirty-five, between the fifth and eighth decades; and only seven were in the second decade of life. No cases in the Kennedy-Moersch series were reported as starting in the first decade of life. But in 1941 Levethan, Fried, and Madonick[5] found nine patients under 19 years and thirty-four below the age of 17. Lieberman[6] has reported the condition in a child of 5 years. As far as we know, the youngest case already on record was reported recently by Kawaichi and Ito[7] in an infant 21 months old. The patient whom we are reporting was 7 years old when first seen, but, basing the opinion on the history obtained from the mother, there is reason to believe that the patient started to show symptoms at a much earlier age, possibly as early as her second year.

It is well known that the disease is more often found in the female sex than in the male. The muscles innervated by the bulbar nuclei are usually most seriously involved and produce symptoms in the facial, in the oculomotor, the muscles of mastication and the neck muscles. When these muscles are affected and the weakness in a pathologic degree is typically induced by repetition of movement, one makes the diagnosis with much assurance on wholly clinical grounds. But there are problematic cases quite difficult to classify which in the early stages have only obscure symptoms of generalized weakness. This type requires differentiation from psychogenic conditions of weakness. An unan-

swered question arises—are there incomplete forms of the condition which remain at a mild generalized stage and fail to extend to the muscles innervated by the bulbar nuclei?

It is well to point out that smooth muscle as well as voluntary muscle can be involved. We can recall being told that there is never any involvement of the pupillary muscles. But this has been disproved.

Dysphagia which occurs in 60 per cent of the cases depends on functioning of the esophagus, the lower third of which is smooth muscle. Schwab and Viets[8] have used the x-rays to study the swallowing reflex in patients with dysphagia. It is a simple and useful form of the prostigmine test. Swallowing of barium is brought back temporarily to normal after a proper amount of the drug is injected in cases of myasthenia gravis and this does not occur in other diseases.

The myasthenia gravis syndrome is characterized by a disorder of the chemical component of neuromuscular transmission. The difficulty occurs at the myoneural junctures and concerns acetylcholine—a chemical substance believed to be essential for the transmission of stimuli from the nerve endings to the muscle fibres. It is not surely established whether it is a disturbance of the liberation of acetylcholine or a too rapid destroying of this substance. Milhorat[9] has studied the latter possibility of the method of determining choline esterase activity and his findings while highly pertinent would not appear to be conclusive. For example, choline esterase activity of the blood serum of patients with myasthenia gravis is found to be not unusual and of the same order as that seen in the large series of patients without the condition. Also, spontaneous changes in muscular disability in patients with myasthenia gravis is not accompanied by changes in esterase activity. On the other hand, in instances of improvement in muscular function which had been induced by prostigmine administration, the improvement was found to be accompanied by a cutting down of esterase. In other words, these investigations to date show a certain disagreement, but it is known that prostigmine facilitates acetylcholine functioning. It produces effects similar to those seen after stimulation of cholinergic fibers and appears to inhibit the destruction of acetylcholine. An additional phase of the chemistry of the disorder bears upon potassium metabolism. It is known that the concentration of potassium ions is important in muscle contraction. This potassium concentration is increased in myasthenia gravis and the degree of muscle weakness appears to be associated with the amount of potassium in the muscles at the time. The drug prostigmine which relieves the weakness causes a decrease of the muscle potassium of the blood.

It is well to recall that not all orders of nerve fibers are capable of liberating acetylcholine, in other words, not all nerve fibers are cholinergic. The differentiation is mostly, though not entirely, along the lines of the sympathetic and the parasympathetic. Krieg[10] gives as modern an account of acetylcholine as we have and describes acetylcho

line as usually a parasympathetic product but adds: "paradoxically in a few situations as in the sweat glands, acetylcholine is regularly the sole product of sympathetic activity. In such a case, a sympathetic fiber produces an effect which is typical of the parasympathetic." He adds: "thus the morphologic division of the autonomic into sympathetic and parasympathetic parts is not quite correct physiologically." Myasthenia gravis, therefore, cannot be put down as a disorder of the parasympathetic. As said before, it rests on cholinergic disturbances which may arise in the sympathetic system as well.

There is a similarity between the symptoms of myasthenia gravis and the response to curare injections—a similarity pointed out first by Bennett.[11] More recently he[12] has described a diagnostic test for myasthenia gravis based on the fact that affected individuals show abnormal curare sensitivity. In five patients, in different stages of the disease, he found that profound exaggeration of the myasthenic symptoms arose after the injection of only one-fifteenth to one-fifth of the average adult dose required to produce generalized muscular paresis. The test is not without danger and must be terminated within two or three minutes by the intravenous injection of 1.5 mg. of prostigmine methylsulfate with 1/100 grain of atropine sulfate. The use of this test is now facilitated by the fact that standardized curare* is now available. There would seem to be small need for this diagnostic test in patients having bulbar nuclei signs and symptoms, but it should prove even more helpful than faradic testing in doubtful cases with muscle weakness arising from spinal levels. Much has been written in the past about creatine metabolism in the disease. Creatinine of the urine is normally derived from the creatine of the muscles. If the creatine of the muscles is not utilized in muscle work, it appears in the urine as a wasted metabolic product. Milhorat's[9] studies in this field are fairly recent and the following is quoted from his article: "Gross changes in the metabolism of creatine in myasthenia gravis (not due to some accompanying condition such as hyperthyroidism) have a grave prognosis for life. On the other hand, the data do not justify the inference that when the metabolism of creatine is normal, the prognosis for life is favorable. Patients with myasthenia gravis who are seriously ill often show no significant change in the metabolism of creatine." It would seem, therefore, that while the creatine-creatinine balance is altered in the disease, the presence of creatinuria can no longer be given the diagnostic importance which it once was thought to hold. For practical purposes the estimation of creatine in the urine can be eliminated.

The pathologic study of the muscles in myasthenia gravis shows the presence in them of so-called lymphorrhages. It is far from clear upon what precise basis these arise and what relationship they hold to the chemical factors of the disease. Not limited to skeletal muscle it is

*Intocostrin prepared in 5 and 10 c.c. vials by E. R. Squibb & Sons, New York, N. Y.

known that some investigators have found them in the myocardium. Weigert[13] first noticed this cardiac muscle involvement in 1901. Others have written of it since, including Mella[14] in 1923 and Rottino, Poppiti and Rao[15] more recently.

Post-mortem studies show tumors, hyperplasia, or enlargement of the thymus in 50 per cent of the cases. The tendency for the thymus to enter the picture was also first observed by Weigert[13] in 1901. Bell[16] in 1917, out of fifty-six cases, found twenty-seven with either thymoma or persistent and enlarged thymus. Norris[17] in 1936, found thirty-five cases with lesions of the thymus in a series of eighty necropsies. It has been pointed out by Campbell and his co-workers,[18] that the thymic tumors are practically always benign and that "malignant thymoma, many cases of which have been reported, rarely, if ever, occurs in conjunction with the disease."

Insufficient data have as yet been collected. But it is coming to be thought that if a patient with myasthenia gravis shows evidence of a thymic enlargement, surgical removal should be strongly considered. A remission of symptoms has followed thymectomy in at least five recorded instances—Sauerbruch,[19] Von Haberer[20] (1917), Blalock and associates[21, 22] (1941), Campbell, Fradkin, and Lipetz[18] (1942), and Poer[23] (1942). In only Blalock's case was it a 100 per cent remission and Blalock points out that the period since the operation is still only five years and admits that an evaluation of the result is difficult due to the known possibility of spontaneous remission. Leriche and Jung[24] performed thymectomy in one patient with no change in symptoms. Blalock refers to thymectomy as a simple operation.

In this connection something should be added regarding the therapeutic irradiation of the thymus gland in these cases. There is a recent report by Aring.[25] He gives the results in three adult women patients. In two, who had been found to have thymic enlargement, the response was striking. In the other with no noticeable thymic enlargement, there was less improvement. One patient had rather complete remission for four years, and the therapy in the other more favorable case returned the patient to almost normal activity and the remission had lasted for nine months. Aring believes that irradiation should always be given a chance but points out that it is not surely known if benefit can be expected when there is no demonstrable thymus enlargement.

Myasthenia gravis does not show usually a familial tendency. Yet there are a few instances in which more than one case has been seen in a family. Riley and Frocht[26] reported the condition in sisters. Clinical oddities turn up, such as a monocular myasthenia gravis reported by Winton.[27] Ptosis of one upper lid was the only sign although the labelling of the case might more accurately suggest involvement of ocular muscles.

Unexplained effects on the disease are sometimes obtained by pregnancy. Viets and associates[29] found that in five patients whom they had an opportunity to watch throughout their pregnancy, all but one showed a complete remission of symptoms during the course of the pregnancy. The change came in the second and third weeks and the relapses came after delivery, in a gradual fashion.

Viets and associates[29] do not say whether the fetuses in these cases were all of one sex and if so, whether male or female. Speculation on the endocrinal possibilities in this situation come to mind but do not warrant any elaboration.

CASE REPORT

F. F., a 7-year-old girl, was first seen in the outpatient department of the Lenox Hill Hospital on June 9, 1943. Her mother, who is quite intelligent, brought her because the child fatigued easily and had a difficulty in speech.

The child, whose birth was a normal spontaneous delivery, was born on May 8, 1936, in the Misiricordia Hospital. There were no complications, such as convulsions, following her birth. She at first progressed normally, sat up at 7 months of age, had her first tooth rather late, at 9 months, and began to walk at 14 months. However, even as she began her walking it was noted that she would fall repeatedly, had to be picked up and rested for a while before she could continue. This symptom has progressed to the degree that the child can walk only about a block. The mother then either carries the child or proceeds after the patient has rested.

When the child began to talk, she showed a difficulty in pronouncing words which at first was attributed to "baby talk." It has persisted and generally the child can be understood only by people who have known her for a long time. This backwardness in speech may be explained in part by the patient's poor intelligence, a phase which will be referred to more fully later. The important feature in respect to the speech is that it becomes especially indistinct when the child is tired.

The mother tends to describe the weakness as "weak spells" and, if her memory can be trusted, they began when the patient was still less than 1 year old. The child first sat up at 7 months. At this time the mother first thought that the child's weakness was not normal. As fatigue came on, the head would fall forward on the chest, and the eyelids would droop. The mother reported that over a period of several months the symptoms were accompanied by temporary crossing of the eyes. For some reason, the involvement of the eye movements did not continue as a symptom. The acute drooping of the upper lids was only an accentuation of a partial drooping which was generally present. The "weak spells" occurred more frequently as the day wore on.

The symptoms progressed and when first seen and before being given any treatment, the child complained of feeling tired continually but with exacerbations already mentioned. She could not take part in games with other children and was unable to attend school normally. More recently home teaching has been arranged for her.

So far there has been no disturbance of swallowing or mastication.

Past history.—The patient was bottle fed and had no feeding problems. She had measles at 6 years without complications. But she has had none of the other diseases of childhood and has had no operations. She has had inoculations for diphtheria and smallpox.

Family history.—The father is living and is in the post-office service. There are three children in the family. The two siblings, 19 and 15 years old, have developed normally and show no signs of the disorder.

There is no known familial background of myasthenia gravis on either the paternal or maternal side.

Physical examination.—F. F. is a thin, pale child of average development for her age. She is 50 inches tall and weighs 51½ pounds. The skin is clear. There are no palpable lymph nodes. No masses are felt in the neck and the trachea is in the midline. There is equal expansion of the chest on the two sides and it is clear on percussion and auscultation. The point of maximal impulse is in the fifth intercostal space at the mid-clavicular line. The heart sounds are normal and there is no thrill. A soft systolic murmur is heard over the pulmonic area. Examination of the abdomen is negative, the liver and spleen show no enlargement, and no masses are palpable. There is no clubbing or cyanosis of the fingers.

Neurologic examination.—The patient is right-handed. Her Rhomberg is negative and her station normal except that in these tests she keeps shifting from one foot to the other and complains of feeling tired. She can stand on her heels, on her toes, and on either leg alone. She can walk a line. Except when in an acutely fatigued stage, she walks normally, though slowly.

The fundi are clear, the pupils are equal, regular in outline, and reactive to light directly and consensually. They react on accommodation. There are normal eye movements and no nystagmus. The upper eyelids show mild bilateral ptosis and this has been seen to vary at different examinations. Sensation over the distribution of the fifth nerve is normal and the muscles of mastication function normally. There is no facial asymmetry. Hearing tests show good acuity. Air conduction is greater than bone conduction on each side. There is normal function in the palatal muscles. The tongue protrudes in the midline and shows no atrophy. The muscles supplied by the eleventh nerve function on testing.

The musculature of the body is fairly well developed and shows no focal atrophies.

The deep reflexes in the arms are alike on the two sides. The abdominal reflexes are active. The knee and ankle reflexes are present and of average strength. The plantar responses are flexion. Sensation is well preserved in all its forms.

Mental testing indicates the child's defective intelligence which we look upon as having no primary, though possibly it does have a secondary, dependence upon the myasthenia gravis. This would rest upon the fact that the illness has hindered the patient's normal association with other children. On the revised Stanford-Binet form L, the range went from 2 years, 6 months to 6 years. The mental age reached was 3 years, 1 month and the Intelligence Quotient was 44. On the Pintner-Cunningham Primary test, form a, the mental age was 5 years, 5 months, and the Intelligence Quotient, 77. It is probable that the higher score with the latter test is due to the fact that, compared to the Stanford-Binet, it is less dependent upon language.

Blood studies.—The blood count is within normal limits.

Hemoglobin, 14.6 Gm.; red blood cells, 4,800,000; white blood cells, 8,800; polymorphonuclears 46 per cent; lymphocytes, 50 per cent; eosinophiles, 4 per cent. The fasting blood sugar is 93 mg. The Wassermann and Kline tests on the blood are both negative.

Spinal fluid.—No examination of the spinal fluid has been made.

Urine.—There are no abnormal findings in the urine. Urinary secretion of creatine has not been determined.

X-ray.—The lungs are clear and the heart not enlarged. Also the x-ray shows no evidence of thymic enlargement.

Electrical studies.—Chronaxie studies of the muscles of the face and of the sternocleidomastoid muscle are within normal range. This is true both before and after the intramuscular injection of prostigmine hydrochloride.

Tests with the faradic current gave the results in terms of contractions before exhaustion was induced (Table I).

TABLE I

MUSCLE		AFTER PROSTIGMINE .75 MG. INTRAMUSCULARLY	
		10 MIN. AFTER	30 MIN. AFTER
Right orbicularis oris	15 contractions	18	50
Left orbicularis oris	52 contractions	76	94
Right frontal	5 contractions	38	135
Left frontal	7 contractions	92	135

Speech.—A further test was carried out along the lines of the diagnostic test of Schwab and Viets[28] for myasthenia gravis. The child was asked to count as far as she could. Without the prostigmine, she could count only to twenty-five and even before she reached this mark, her words were quite indistinct. But after the injection of prostigmine (.75 mg.) she counted well above one hundred and enunciated more clearly and distinctly. Improvement was always evident within ten minutes after the injection.

Course.—The child was first placed on a daily oral intake of 15 mg. of prostigmine bromide which was divided into three doses. Her mother reported only slight improvement but the effect was somewhat better when the prostigmine was increased to 22 mg. a day. She was continued on the 22 mg. for two weeks and then ephedrine sulfate 15 mg. a day was added but this brought no particular benefit. Because the patient had responded especially well, as would be expected, to the intramuscular injections, it was decided to give the prostigmine, at least in part, by this method. For many weeks, in addition to a daily dose of 22 mg. orally, she has received .75 mg. intramuscularly every other day. She responds well to this regime and at present is much improved.

In closing, it is well to emphasize that myasthenia gravis is still an unsolved medical problem. It is a problem in itself and in its relationship to other so-called myopathies, especially the group consisting of myotonia congenita, myotonia atrophica, paramyotonia, progressive muscular dystrophy, and periodic paralysis. Two or more of these conditions have been observed in a single individual and certain instances have linked myasthenia gravis into the chain.

Chemistry centering in acetylcholine is altered in myasthenia gravis but the full relationship of this to endocrinal glands and particularly to the thymus gland is still unsolved as is the significance of the lymphorrhages seen in certain muscles at necropsy.

REFERENCES

1. Grinker, Roy R.: Text Book of Neurology, ed. 3, Springfield, Ill., 1943, Charles C Thomas.
2. Remak, E.: Arch. f. Psychiat. **23:** 919, 1891.
3. Gerstle, M., Jr.: California and West. Med. **30:** 113, 1929.
4. Kennedy, F. S., and Moersch, F. P.: Canad. M. A. J. **36:** 216, 1937.
5. Levethan, S. T., Fried, A. J., and Madonick, M. J.: Am. J. Dis. Child. **61:** 770, 1941.
6. Lieberman, A. T.: J. A. M. A. **120:** 1209, 1942.
7. Kawaichi, G. K., and Ito, P. K.: Am. J. Dis. Child. **63:** 354, 1942.
8. Schwab, R. S., and Viets, H. R.: Am. J. Roentgenol. **45:** 357, 1941.
9. Milhorat, A. T.: Arch. Neurol. and Psychiat. **46:** 800, 1941.
10. Krieg, W. J. S.: Functional Neuroanatomy, Philadelphia, 1942, The Blakiston Co.

11. Bennett, A. E.: Am. J. M. Sc. **202**: 102, 1941.
12. Bennett, A. E., and Cash, P. T.: Arch. Neurol. and Psychiat. **49**: 537, 1943.
13. Weigert, C.: Neurol. Centralbl. **20**: 597, 1901.
14. Mella, H.: M. Clin. North America **7**: 939, 1923.
15. Rottino, A., Poppiti, R., and Rao, J.: Arch. Path. **34**: 557, 1942.
16. Bell, E. T.: J. Nerv. & Ment. Dis. **45**: 130, 1917.
17. Norris, E. H.: Am. J. Cancer **27**: 421, 1936.
18. Campbell, E., Fradkin, N. F., and Lipetz, B.: Arch. Neurol. and Psychiat. **47**: 645, 1942.
19. Sauerbruch, cited by Schumacher and Roth: Mitt. a. d. Grenzgeb. d. Bed. u. Chir. **25**: 745, 1913.
20. Von Haberer, H.: Arch. f. klin. Chir. **109**: 193, 1917.
21. Blalock, A., Mason, M. F., Morgan, H. J., and River, S. S.: Ann. Surg. **110**: 544, 1939.
22. Blalock, A., Harvey, A. M., Ford, F. R., and Lilienthal, J. L., Jr.: J. A. M. A. **117**: 1529, 1941.
23. Poer, D. H.: Ann. Surg. **115**: 586, 1942.
24. Leriche, R., and Jung, A.: Mem. Acad. de chir. **65**: 334, 1939.
25. Aring, C. D.: Ohio State Med. J. **39**: 241, 1943.
26. Riley, H. A., and Frocht, M.: Arch. Neurol. and Psychiat. **49**: 904, 1943.
27. Winton, S. S.: J. A. M. A. **122**: 1180, 1943.
28. Schwab, R. S., and Viets, H. R.: New England J. Med. **219**: 226, 1938.
29. Veits, H. R., Schwab, R. S., and Brazier, Mary A. B.: J. A. M. A. **119**: 236, 1942.

CONGENITAL AND INFANTILE BERIBERI

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RECENTLY we have observed a newborn infant who exhibited the clinical features described for congenital beriberi. A review of the literature failed to disclose any cases reported from an occidental country. Beriberi is much more serious in infants than in adults, and dramatic results follow specific treatment.

Although beriberi was known to the Romans as early as 24 B.C., Hirota[1] in 1888 was the first observer to describe the infantile form of beriberi. Since that time there have been numerous reports, particularly from the Orient, referring to the infantile type. In 1928 the report of the Committee on Beriberi in the Philippines[2] indicated that there were 16,500 infantile deaths annually from this disease. This number represented 28.1 per cent of the total deaths among infants under 1 year of age in that territory. According to Ching-lang[3] in Japan beriberi ranked sixth in the list of causes of infant deaths. In this country Haas[4] in 1929 presented four cases of children in late infancy with evidence of vitamin B_1 deficiency associated with celiac disease. Waring[5] observed four infants with beriberi. The youngest infant, 2 months of age, had cardiac enlargement. Abt[6] considered the possibility of vitamin B_1 deficiency in infants with cardiac enlargement. Rascoff[7] described a 4-month-old infant with a beriberi heart due to an inadequate diet.

Although congenital beriberi has been mentioned frequently, the number of case reports is extremely limited. Ohta[8] saw congenital beriberi only once out of 430 cases of infantile beriberi. Albert[9] noted that congenital beriberi is exceptionally rare; it occurred only four times in his series of 514 infants with beriberi. Ching-lang[3] reported having seen several infants with congenital beriberi and stated that the symptoms often develop on the third or fourth day of life. Case reports are given for two infants. One infant had symptoms since birth and was seen on the third day of life; the other child was 13 days old at the time of observation. In the first case the only signs the mother exhibited were some tenderness of the thighs and moderate edema during the latter part of her pregnancy. Mata[10] cited briefly an infant 3 days old who was cyanotic, dyspneic, and in apparent pain. The mother had some edema and diminished deep tendon reflexes. One hour after the injection of 10 mg. of thiamine the baby was reported to be free from pain.

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DESCRIPTION OF VITAMIN B_1 DEFICIENCY STATES IN INFANTS

The manifestations of beriberi in the infant are protean, and the symptomatology differs considerably from that resulting from vitamin B_1 deficiency in adults. The dry type of beriberi is uncommon among infants, and although Albert[9] states that multiple peripheral neuritis, so frequently seen in adults, is unknown in the infant, we believe that neuritis would be difficult to exclude at this age.

The prenatal history often reveals that the mother has had mild palpitation, numbness or tingling in the hands and feet, some tenderness of the calf muscles, and slight edema. Usually the mother has had an inadequate diet, frequently consisting mainly of refined carbohydrates.

The infantile form of beriberi usually develops when the child is 2 to 3 months of age, although it may occur later in infancy. It has been repeatedly observed in the orient that the vast majority develop in babies who are breast fed. This observation has given rise to the theory that "toxic breast milk" produces the symptomatology. The milk of B_1 avitaminotic mothers supposedly lacks not only the vitamin but also contains a poisonous substance.[11] This toxin was found to be related to methylglyoxal,[12] an intermediate product in the metabolism of carbohydrates. It has been a common observation that the severity of the disease in the infant bears no relationship to its severity in the mother. The infant may be critically ill although the disease may be latent or subclinical in the mother.

Bray[13] has given an excellent description of the symptomatology of vitamin B^1 deficiencies in the infant. In the chronic form (infantile pre-beriberi), the infant is often apathetic. Anorexia is present, associated with vomiting, constipation, or occasionally diarrhea. The muscles are deficient in tone, and the infant may appear fat and flabby. In the more acute types he recognized three phases. The first, or gastroenteric phase, is characterized by anorexia, restlessness, colicky pains, abdominal tenderness and distention, regurgitation or vomiting, and oliguria. The infant may gain weight and appear well nourished, but this misleading finding is due to edema. As the disease progresses, the pneumonic phase develops. In this stage the infant becomes cyanotic and dyspneic, the heart rate becomes rapid, the liver may be enlarged, and the area of cardiac dullness increases. The cry which at first is feeble finally is lost. The aphonia apparently is due to irritation and degeneration of the fibers of the vagus nerve which innervate the larynx.[14] In the final, or meningismic phase, evidence of meningeal irritation is present. The anterior fontanel bulges and opisthotonos with bodily rigidity is observed. Occasionally the patellar reflexes are diminished. These symptoms may be followed by convulsive movements, coma, and death. Spinal puncture fails to alleviate the symptoms.

It is difficult to establish a diagnosis by means of laboratory tests unless a specialized laboratory is available. Thiamine assays of the urine, blood pyruvic acid levels, and possibly lactate-pyruvate ratios in the blood may establish the diagnosis of vitamin B_1 deficiency, but unfortunately none of these assays are available in the average clinical laboratory. There is nothing characteristic about the blood picture, although Shindo[15] states that in most cases there is an anemia, neutropenia, and thrombocytosis which is usually corrected by administration of vitamin B.

The response following the administration of thiamine is spectacular. Frequently it is a matter of only a few hours before an improvement is noted. No adequate explanation has ever been given for the predominantly right-sided enlargement of typical "beriberi heart." However, since the reduction in cardiac size with adequate therapy is often so rapid, it would seem logical that a portion of the cardiac dilatation seen radiographically is due to interstitial edema. Sosman[16] states that a legitimate diagnosis of a beriberi heart may be made when a rapidly beating, dilated heart slows and becomes smaller after administration of vitamin B.

We have, then, apparently adequate data for the recognition of congenital beriberi. According to some writers, it is only surprising that more clinical examples are not recognized. It is the purpose of this communication to describe the sequence of events leading us to believe that we have encountered a case of congenital beriberi recently, to point out the clinical features by which one could suspect its occurrence in the future, and to recommend adequate therapy in suspected cases.

REPORT OF CASE

Maternal History.—Prior to the time of our observation, three months before delivery, the mother, a primipara, had been under the care of another physician. According to his reports, urinalyses were negative, the hemoglobin was 80 per cent (Tallqvist), the red blood count was 5,180,000, and the Wassermann test was negative. The blood pressure July 1, 1943, was reported as 146/90, and Aug. 5, 1943, it was 140/80.

At the time of initial examination by one of us (F. D.) Sept. 2, 1943, physical examination of the mother was negative except for a mild edema of the face and extremities. Urine was normal, and blood pressure was 130/80. Because of edema the mother was advised to limit her fluid intake to 750 c.c. daily and to reduce her salt intake. The mother followed this advice but also voluntarily limited her diet to apples, bananas, grapes, grapefruit, tomatoes, raw turnips, and approximately six slices of white bread with less than one glass of milk daily. At subsequent examinations blood pressure and urinalyses remained normal, but edema persisted unchanged in degree. The mother's total weight-gain during her pregnancy was 34 pounds, and during the last trimester she complained of mild numbness and tingling in her hands and feet.

Birth History.—The birth of patient, T. E., Dec. 18, 1943, was normal. The mother was in labor thirteen hours and forty-five minutes. The fetus was in a vertex presentation, left occiput anterior. The birth weight was 7 pounds, 5 ounces. Immediately after birth it was noted that the baby was cyanotic, but the

color rapidly improved following the use of a resuscitator. However, three hours after delivery the baby again became cyanotic, requiring administration of oxygen.

Initial Physical Examination.—The physical examination revealed a plump, apparently well-nourished, white male infant who was cyanotic about the lips and extremities. The eyes, ears, nose, and throat appeared normal. A few fine crackling râles were heard over the bases of both lung fields posteriorly. The area of cardiac dullness was increased to percussion. The heart rate was so rapid that the apex beat could not be counted. The liver edge was palpable, but the liver did not appear to be enlarged. The neurologic examination was normal.

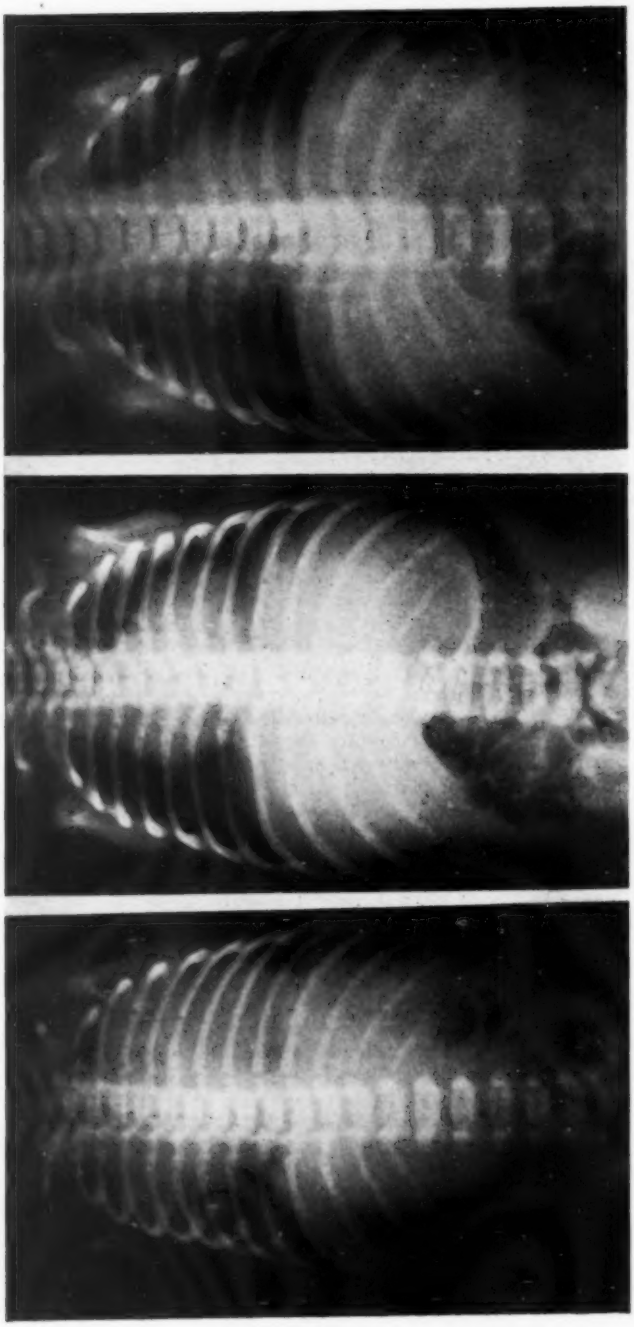
Clinical Course.—An x-ray picture of the chest, taken at 18 hours of age, revealed an enlarged heart (Fig. 1*A*). During the first day of life, despite continuous administration of oxygen, the infant had several cyanotic attacks. Three minims of coramine were given subcutaneously during two attacks without any discernible effect. On the second day of life it was noted that the cry was hoarse and very feeble. The cyanotic attacks became more frequent and severe. When the baby was 30 hours old, the head became retracted, and convulsive movements with rigidity of the extremities developed. During this time feeding difficulties were encountered, characterized mainly by refusal to take an ordinary evaporated milk dextrimaltose formula. Fifty cubic centimeters of 5 per cent glucose in saline were administered subcutaneously twice a day during the first four days of life.

When the infant was 42 hours old, an initial dose of 50 mg. of thiamine hydrochloride was administered subcutaneously. A second similar dose was administered eight hours later. About four hours after the first dose of thiamine hydrochloride the convulsive movements ceased, but the cyanosis persisted. Twelve hours after the second dose of vitamin B_1, however, the baby appeared dramatically improved. The color was normal, and no further cyanotic attacks were noted. At this time he began to suck on a dropper feeder, and the cry although still hoarse was considerably stronger. Thiamine hydrochloride in 50 mg. doses was continued every eight hours for a period of eleven days without any apparent toxic effects. On the third day following the initial administration of thiamine hydrochloride physical examination of the chest revealed reduction of the area of cardiac dullness. The heart rate was reduced to 160 beats per minute. The blood pressures were 98/74 in the right leg and 96/72 in the left leg. On Dec. 24, 1943, four days after thiamine therapy was instituted, an electrocardiogram (Fig. 2, *A*) was taken, revealing a sinus tachycardia, right axis deviation, and complexes of low voltage in all leads. Dr. J. L. Gouaux, consulting cardiologist, interpreted this tracing as showing definite evidence of myocardial disease.

After the fifth day of life, the infant took three ounces of formula at each feeding. When the baby was reweighed Dec. 27, 1943, his weight was 6 pounds, 15 ounces, which was only 6 ounces under his birth weight. The lowest weight, 6 pounds, 9 ounces, was recorded on the twentieth day of life. It was noted that despite an adequate caloric intake with clinical improvement the infant lost his plump, well-nourished appearance. However, no abnormalities of urination were noted at any time. The only other finding was a moderate, apparently physiologic jaundice which appeared on the third day after birth and persisted through the third week of life.

An x-ray of the chest taken Dec. 31, 1943 (Fig. 1, *B*), twelve days after the first film, showed a marked reduction in the size of the cardiac shadow. A second electrocardiogram (Fig. 2, *B*), taken at 7 weeks of age, appeared to be normal except for sinus tachycardia.

Thiamine hydrochloride was gradually reduced to 50 mg. daily by the third week of life. At this time the pulse rate was 130 per minute. The parenteral use of thiamine hydrochloride was discontinued, and an oral preparation of vitamin B complex was started which contained 3 mg. of thiamine hydrochloride in the daily



A. *B.* *C.*

Fig. 1.—*A*, X-ray picture taken Dec. 19, 1943, before thiamine therapy was instituted. *B*, X-ray picture taken Dec. 31, 1943, eleven days after administration of first dose of thiamine. *C*, X-ray picture taken on Feb. 12, 1944, fifty-four days after first dose of thiamine.

dose. Shortly after the parenteral use of thiamine was discontinued the heart rate rose to 160 beats per minute, but with continued use of vitamin B by mouth for one month the rate dropped to 135 beats per minute. On Feb. 12, 1944, an x-ray picture of the chest showed a normal-sized heart (Fig. 1, *C*). The physical examination at this time was apparently normal, and the infant's weight was 8 pounds, 13 ounces. At 3 months of age, however, searching movements of the eyes were noted. The pupils were dilated and homogeneous, apparently soft opacities of both lenses were observed. (In all probability the cataracts were present at birth and possibly were due to the metabolic disturbance resulting from the vitamin B_1 deficiency during intrauterine life.)

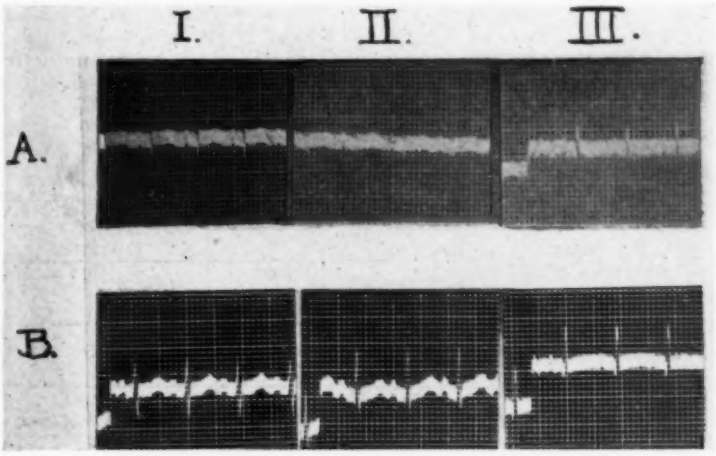


Fig. 2.—*A*, Electrocardiogram taken Dec. 24, 1943, four days after thiamine therapy was instituted; rate: auricle, 170 per minute; ventricle, 170 per minute; P-R interval, 0.08 seconds, QRS, 0.03 seconds. (The standardization was inadvertently omitted from this record except in Lead III. Interpretation given in text as though the standardization were correctly recorded.)

B, Taken Feb. 2, 1944, forty-four days after thiamine therapy was instituted; rate: auricle, 160 per minute; ventricle, 160 per minute; P-R interval, 0.10 seconds; QRS, 0.05 seconds.

Laboratory Data.—Urinalyses were negative Jan. 8 and 11, 1944. The blood picture Dec. 12, 1943, showed a hemoglobin of 80 per cent (Tallqvist); red blood count of 5,900,000; white blood count of 29,100 with 75 per cent polymorphonuclears, 20 per cent small lymphocytes, 3 per cent eosinophiles, and 2 per cent large monoculears. On Jan. 15, 1944, serum calcium was 11 mg. per 100 c.c.; serum phosphorus, 5 mg. per 100 c.c.; blood cholesterol, 180 mg. per 100 c.c.; and Wassermann test was negative. A dextrose tolerance test done Jan. 22, 1944, gave the following results: a fasting level of 70 mg. per 100 c.c. of blood; blood levels after ingestion of 6 Gm. glucose at one-half hour, 130 mg. per 100 c.c.; at one hour, 140 mg. per 100 c.c.; and at two hours, 102 mg. per 100 c.c.

Observations on the Mother.—Unfortunately no pertinent tests were done for the mother during the immediate postnatal period when her thiamine deficiency was undoubtedly most evident. A few days after delivery the mother's edema had disappeared, but at this time she was taking a well-balanced hospital diet which contained adequate amounts of thiamine. In addition, the added requirements of thiamine, due to pregnancy, had now been removed. During the second post-partal week, however, the mother developed a mild cheilosis. This evidence of ariboflavinosis persisted for ten days.

For three and one-half weeks after the birth of her infant, the mother's diet was entirely adequate in vitamin requirements. Then for the next two weeks she was given a diet limited to the same foods she had taken during the last trimester. At the end of this period thiamine assays of urine were done by the thiochrome method. The total thiamine content of a twenty-four-hour urine sample (of 490 c.c.) was 19.6 μg. A four-hour urine sample, collected after the subcutaneous injection of one mg. of thiamine hydrochloride, contained 159.33 μg (Table I). Dextrose, pyruvic acid, and lactic acid blood levels were also done at the end of the two-week period of dietary limitation. The subject was at rest in bed while these tolerance tests were done. The fasting blood level for dextrose was 76 mg. per 100 c.c.; for pyruvic acid, 1.1 mg. per 100 c.c.; and for lactic acid, 8 mg. per 100 c.c. One hour after the ingestion of 70 Gm. of dextrose the blood levels were 153 mg. per 100 c.c. for glucose, 1.3 mg. per 100 c.c. for pyruvic acid, and 7.9 mg. per 100 c.c. for lactic acid. The two-hour blood sample showed a level for dextrose of 166 mg. per 100 c.c., pyruvic acid, 1.5 mg. per 100 c.c., and lactic acid 10 mg. per 100 c.c. (Figs. 3 and 4).

TABLE I

MATERNAL THIAMINE EXCRETION

URINARY THIAMINE ASSAYS	AVERAGE DAILY SAMPLE		4-HOUR SAMPLE (AFTER INJECTION OF 1 MG. OF THIAMINE)	
	VOLUME (C.C.)	THIAMINE CONTENT (μG)	VOLUME (C.C.)	THIAMINE CONTENT (μG)
On prenatal diet (for 2 weeks)	490	19.6	47	159.33
On adequate diet plus 60 mg. Thiamine daily (for 2 weeks)	650	952.5	300	210

After this preliminary two-week period of dietary restriction, the mother received an adequate well-balanced diet with a supplementary oral dose of 60 mg. of thiamine hydrochloride daily. Two weeks later similar urinary thiamine assays and blood tolerance tests were done. Inadvertently the mother collected a forty-eight-hour urine sample, and collection was started about twenty hours after the last supplementary oral dose of thiamine. An average daily sample (of 650 c.c.) contained 952.5 μg of thiamine, but a portion of this amount undoubtedly represented excess excretion as a result of the large oral doses of thiamine taken prior to the collection. At the end of the forty-eight-hour period of collection 1 mg. of thiamine hydrochloride was injected. The subsequent four-hour urine sample contained 210 μg of thiamine (Table I). The fasting blood levels were for dextrose 94 mg. per 100 c.c., for pyruvic acid 0.5 mg. per 100 c.c., and for lactic acid 5.7 mg. per 100 c.c. Levels one hour after the ingestion of dextrose showed: dextrose 126 mg. per 100 c.c., pyruvic acid 1.1 mg. per 100 c.c., and lactic acid 11.2 mg. per 100 c.c. Two-hour levels were 110 mg., 1.1 mg., and 12.8 mg. per 100 c.c., respectively (Figs. 3 and 4).

The daily urinary excretion of thiamine after the two-week period of dietary restriction was within the range of a minimal deficiency. However, excessive amounts of thiamine were excreted after the diet was corrected. "Load tests" performed following the subcutaneous injection of 1 mg. of thiamine, showed an increase in the fraction of thiamine recovered after the period of adequate thiamine intake (Table I).

The first dextrose tolerance test is definitely abnormal, but following the intake of adequate amounts of thiamine, this tolerance test became normal (Fig. 3). While the subject was on her prenatal diet, the blood pyruvate level was highest two hours after dextrose ingestion. Bueding and associates[18] state that in normal individuals the elevation in blood pyruvic acid invariably reaches a maximum one

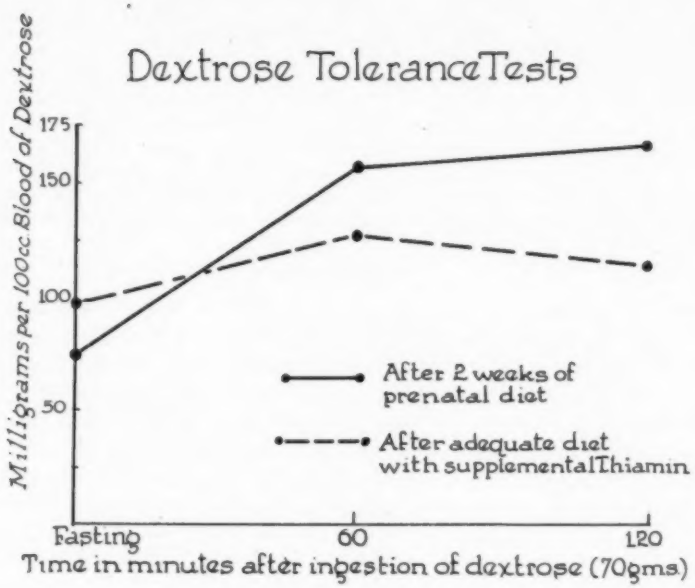

Dextrose Tolerance Tests
Milligrams per 100cc Blood of Dextrose
175
150
100
50
After 2 weeks of prenatal diet
After adequate diet with supplemental Thiamin
Fasting
60
120
Time in minutes after ingestion of dextrose (70gms)

Fig. 3.

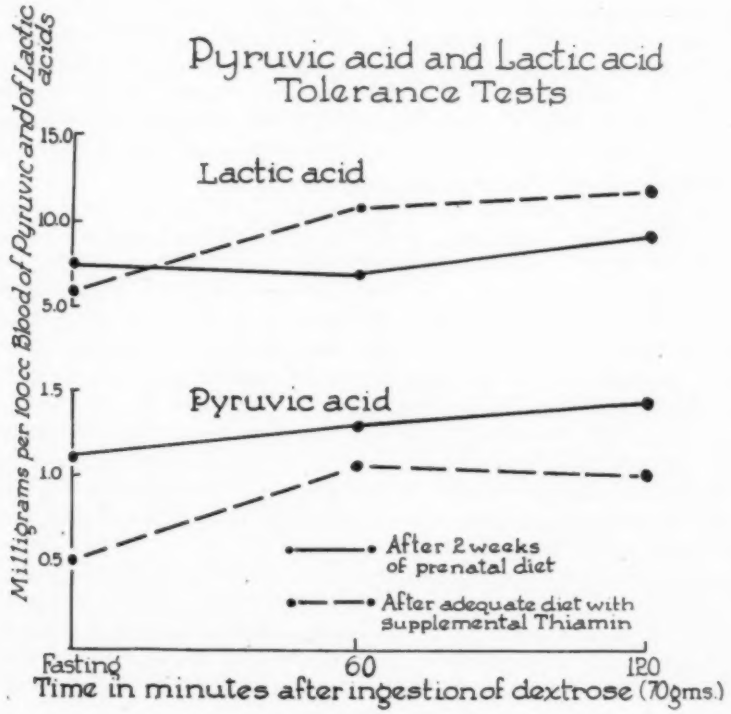

Pyruvic acid and Lactic acid Tolerance Tests
Milligrams per 100cc Blood of Pyruvic and of Lactic acids
15.0
10.0
5.0
Lactic acid
1.5
1.0
0.5
Pyruvic acid
After 2 weeks of prenatal diet
After adequate diet with supplemental Thiamin
Fasting
60
120
Time in minutes after ingestion of dextrose (70gms.)

Fig. 4.

hour after ingestion of dextrose. The pyruvic acid values were reduced after the mother's diet was corrected (Fig. 4). The lactate: pyruvate ratio, which has been suggested as a diagnostic aid in the determination of thiamine deficiency, was low following the period of dietary restriction, while normal values were found after the diet had been corrected. Dr. G. A. Goldsmith,[19] of the Department of Medicine of Tulane University felt that these findings in conjunction with the urinary thiamine assays were indicative of thiamine deficiency during the period of dietary restriction.

COMMENT

Despite a wholly inadequate prenatal diet, the mother did not exhibit any marked clinical findings of beriberi. Although the mother had an apparent subclinical attack of beriberi, the infant was born with severe, almost fatal manifestations. It is difficult to explain this difference in degree of objective evidence of avitaminosis between mother and infant, but the case illustrates well that one should be on guard when a pregnant woman has been subsisting on a poor diet. Burke and associates[20] have shown a statistically significant relationship between the diet of the mother during pregnancy and the condition of the infant at birth.

The slight edema that the mother exhibited during the last trimester was originally considered to be due to a mild toxemia of pregnancy despite normal blood pressures and negative urinalyses during this time. It might be a wise procedure in similar cases to employ parenteral vitamin B_1. It is a well-known fact that pregnancy or lactation increases the vitamin B_1 requirements two or three times. We believe that in addition to supplementing the diet with minerals and other vitamins during pregnancy and lactation, an adequate daily oral dose of a vitamin B complex should also be given.

Kugel and Stoloff,[21] in a review published in 1933, found only seventeen cases which apparently fitted the description of congenital idiopathic cardiac hypertrophy. Rosen[22] concluded that there was no such entity as idiopathic congenital cardiac hypertrophy. It is very likely that some cases diagnosed as such are actually unrecognized beriberi. Furthermore, it is entirely possible that some of the case reports of children, that have been thrown into the catchbasket of so-called "status thymicolymphaticus," may be undiagnosed congenital or infantile beriberi. Thiamine hydrochloride in extremely large doses was administered to this infant; nevertheless, no evidence of toxicity was demonstrated. We believe that infants with large hearts, in whom no valvular or congenital lesion can be demonstrated, should receive large parenteral doses of thiamine hydrochloride as a therapeutic test.

Knott and associates[23] have shown that breast milk may not meet the thiamine requirement of the infant. We believe that if analysis of the mother's diet indicates any justification for suspecting inadequacy, supplementary doses of a vitamin B complex, in addition to other vitamins, should be given to the nursing infant until such time as other foods containing vitamin B are introduced.

SUMMARY AND CONCLUSIONS

1. A brief review of the literature on congenital and infantile beriberi is given with a description of thiamine deficiency states in infants.

2. A case of congenital beriberi is reported. The infant was cyanotic and almost aphonic, with extreme tachycardia and a greatly enlarged heart. Spectacular improvement resulted from the use of large parenteral doses of thiamine hydrochloride. Radiographs and electrocardiograms are presented.

3. Urinary thiamine assays and dextrose, pyruvate and lactate blood levels, fasting and following ingestion of dextrose, indicated a state of thiamine deficiency in the mother.

4. It is considered that some cases of "congenital idiopathic cardiac hypertrophy" or "status thymicolymphaticus" may actually be instances of unrecognized congenital or infantile beriberi.

5. Infants with large hearts in whom no valvular or congenital lesion can be demonstrated should be given large parenteral doses of thiamine hydrochloride as a therapeutic test.

6. During pregnancy and lactation a mother should be provided with an adequate intake of vitamin B. If the maternal diet is suboptimal, the nursing infant should receive additional vitamin B_1 until such time as other foods containing this vitamin are introduced.

We wish to acknowledge our thanks to Dr. E. A. Feiger of Louisiana State University for performing the thiamine assays in the Nutrition Research Laboratory. We also wish to express our appreciation to Dr. G. A. Goldsmith of Tulane University School of Medicine for determining the pyruvate and lactate blood levels.

REFERENCES

1. Hirota, J.: Jika hikkei, Tokio, 1888.
2. Lopez, R.: J. Philippine Islands M. A. **8:** 422, 1928.
3. Ching-lang, K.: China Med. J. **50:** 324, 1936.
4. Haas, S.: Arch. Pediat. **46:** 467, 1929.
5. Waring, J.: Am. J. Dis. Child. **38:** 52, 1929.
6. Abt, I.: Am. J. Dis. Child. **50:** 455, 1935.
7. Rascoff, H.: J. A. M. A. **120:** 1292, 1942.
8. Ohta, H.: Jahrb. f. Kinderh. **128:** 1, 1930.
9. Albert, J.: Philippine J. Sc. **45:** 297, 1931.
10. Mata, C.: J. Philippine Islands M. A. **19:** 493, 1939.
11. Asakura, K., and Oksako, H.: Tohoku J. Exper. Med. **20:** 429, 1933.
12. Takamatsu, A.: Tohoku J. Exper. Med. **23:** 46, 1934.
13. Bray, G.: Tr. Roy. Soc. Trop. Med. & Hyg. **22:** 9, 1928.
14. Alcantaro, V., and Ocampo, G.: Arch. Otolaryng. **30:** 389, 1939.
15. Shindo, M. : Tohoku J. Exper. Med. & Hyg. **38:** 403, 1940.
16. Sosman, M.: Radiology **41:** 351, 1943.
17. Robinson, W., Melnick, D., and Field, H.: J. Clin. Investigation **19:** 399, 1940.
18. Bueding, E., Stein, M., and Wortis, H.: J. Biol. Chem. **140:** 697, 1941.
19. Goldsmith, G.: Personal Communication.
20. Burke, B., Beal, V., Kirkwood, S., and Stuart, H.: Am. J. Obst. and Gynec. **46:** 38, 1943.
21. Kugel, N., and Stoloff, E.: Am. J. Dis. Child. **45:** 828, 1933.
22. Rosen, A.: Am. J. Dis. Child. **65:** 905, 1943
23. Knott, E., Kleiger, S., and Schlutz, F.: J. PEDIAT. **22:** 43, 1943.

500 REYMOND BUILDING

COMBINED IMMUNIZATION AGAINST DIPHTHERIA, TETANUS, AND PERTUSSIS

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THE value of active immunization against certain of the communicable diseases of childhood is no longer questioned by the medical profession, nor by a large portion of the general public. Further progress toward the ideal goal of universal immunization should be hastened by any simplification of technique which saves the time of the physician or, more important, makes the procedure more attractive to the public.

The combination of diphtheria and tetanus toxoids was a step in this direction, now accepted as an altogether feasible and desirable application of the idea of multiple immunization. The present study is concerned with the possibility of combining with the above antigens the concentrated pertussis phase I vaccine. For this purpose, a series of sixty-four children were treated with this triple antigen and their blood sera titrated for its content of diphtheria and tetanus antitoxin and for its agglutinating powers against the pertussis organism.

Procedure.—The material used was a mixture of the fluid toxoids of diphtheria and tetanus, prepared in the usual manner according to the regulations of the National Institute of Health. After detoxification, testing for sterility, and purification, phase I pertussis vaccine was added, the final concentration yielding the usual dose of the two toxoids plus 40,000 million pertussis organisms per cubic centimeter. Thereafter both safety and immunity tests were again done on animals.

The children treated were unselected representatives of our private practice. They were all between 1 and 2 years of age, most of them between 12 and 15 months. They were given 0.5 c.c., 1 c.c., and 1 c.c. doses subcutaneously in the deltoid region at about four-week intervals. Blood was drawn for laboratory testing three months after the last injection.

Reactions.—Reactions were practically nonexistent, despite our fears that a multiple antigen might create a cumulative reaction from its ingredients. In no instance did the mother feel it worth while to call to report untoward symptoms, though all knew the procedure was new and were requested to make such a report. On questioning it developed that a few children were fussy and seemed to have a little tenderness at the site of the injection. There were no lumps or nodules found. This freedom from reactions has continued through a much larger series of patients treated since the ones here reported, and also

The material used in this study was furnished and the laboratory work done by the Cutter Laboratories, Berkeley, California.

with others given a different antigen in which the two toxoids are adsorbed on aluminum hydroxide; this last group has, however, produced painless nodules rather frequently.

Results.—Results can be interpreted only from the evidences of immunity shown by laboratory findings in Tables I, II, and III; some of

TABLE I

PERTUSSIS AGGLUTINATIONS

TITER	NUMBER OF PATIENTS
1:80	3
1:160	4
1:320	5
1:640	17
1:1280	27
1:2560	4
1:5120	4
Total	64

TABLE II

TETANUS TITRATIONS

UNITS ANTITOXIN (PER C.C.)	NUMBER OF PATIENTS
$> 0.1 < 0.3$	1
$> 0.3 < 1.0$	6
1.0	17
$> 1.0 < 3.0$	25
3.0	4
$> 3.0 < 10.0$	6
Not tested (qns*)	5
Total	64

*Insufficient serum.

TABLE III

DIPHTHERIA TITRATIONS

UNITS ANTITOXIN (PER C.C.)	NUMBER OF PATIENTS
$> 0.03 < 0.1$	15
0.1	10
$> 0.1 < 0.3$	10
0.3	2
$> 0.3 < 1.0$	17
1.0	2
$> 1.0 < 3.0$	4
3.0	2
Not tested (qns)	2
Total	64

the patients have been exposed to whooping cough without contracting the disease, but their number is insignificant. The question of the correlation between actual clinical immunity and the laboratory evidences of it is beyond the scope of this report; but it will be seen that our laboratory results with the mixed antigen compare favorably with those expected when each antigen is given separately.

Comment.—Possibly the greatest advantage in this method of combining immunization procedures into three injections is the marked decrease in parental reluctance to having their children immunized. This is particularly true of the tetanus immunization. Most parents feel that it is not necessary when it is offered as a separate procedure, but are quite pleased to find that it can be offered as a bonus along with the ones they have learned to expect. The same increase in cooperation also appears to a lesser extent with the other two diseases.

Conclusions.—Though this series of cases is not large, the consisteney of its results indicates that combined immunization against diphtheria, tetanus, and pertussis is safe, effective, and easy; and it is suggested that its use might result in an increase in the number of children protected against these diseases.

ERYTHROBLASTOSIS FETALIS

A Case Report

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THE present term erythroblastosis fetalis represents a composite of three formerly described conditions; namely, hydrops fetalis, icterus gravis neonatorum, and congenital anemia of the newborn infant.

The condition may be present at birth, at which time generalized edema, jaundice, or anemia may be the presenting signs, either one or all. The amniotic fluid is frequently yellow at the time of delivery, as may be the vernix caseosa. Physical examination will usually reveal a jaundiced, pale infant. The spleen may or may not be enlarged. Blood studies are characterized by a marked decrease in the total red count and hemoglobin, with a predominance of erythroblasts in the smear. The blood will show the presence of the Rh factor.

Evidence of the disease at birth is not always typical, as at times appearance may be delayed from two to five days, at which time anemia and progressively increasing jaundice may be observed.

Various etiologic theories, such as the existence of persistent blood-forming foci, mutation, exhaustion of a maternal hormone for stimulation of fetal blood formation, and the sensitization of the fetus to antibodies in the mother's blood,[1] have been propounded.

In 1940, Landsteiner and Wiener[2] reported on an agglutinin developed in rabbits by injecting blood from the rhesus monkey. When tested with human blood this agglutinin demonstrated the presence of a new substance in human red cells called the Rh factor. About 86 per cent of human blood contains this factor, while 14 per cent does not. The agglutinin is called the anti-Rh agglutinin. Levine, Katzin, and Burnham[3] first reported this agglutinin to be the destructive antibody responsible for the manifestations of erythroblastosis fetalis.

It is now believed that the syndrome arises in Rh-negative mothers who are carrying an Rh-positive baby, whereby a break occurs in the placental barrier, allowing fetal Rh-positive blood to enter the mother's circulation. The existence of this Rh-positive blood in the Rh-negative mother causes the production of an anti-Rh agglutinin which is retransmitted through the placenta into the fetal circulation, where it stimulates the blood-destructive process. This chain of events is also thought to be the causative factor in the occurrence of severe transfusion reactions in those women in whom compatible blood was thought to have been used. In these cases it is postulated that they, being Rh-

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negative, had received one or more previous Rh-positive transfusions which produced the isoagglutinin. This in turn proved incompatible with succeeding transfusions of Rh-positive blood with resulting reaction.

In studying the family histories in erythroblastosis it is interesting to note that the first pregnancy has usually resulted in the birth of a normal infant, but that subsequent pregnancies have terminated in miscarriage or in the delivery of erythroblastotic babies. In the light of this observation, it is suggested that when confronted with a pregnant patient giving such a history, the possibility of delivering an erythroblastotic baby be anticipated in order that Rh-negative blood be available for immediate transfusion.

There is no way of preventing the development of erythroblastosis and it is not known why it occurs in some Rh-negative mothers and not in others. Transfusion accidents in women can be prevented, however, by using Levine's[3] modified cross-matching technique, consisting of incubating a mixture of donor's cells and recipient's serum at body temperature for thirty minutes. The mixture is then centrifuged and read as in the Landsteiner method. Where incompatibility is determined, only Rh-negative blood or blood plasma should be used.

The treatment of this disease consists in the administration of Rh-negative blood, usually given to infants on the basis of 10 c.c. per pound of body weight. Mother's blood, however, cannot be used, since it contains the antiagglutinin. Some difference of opinion exists as to the advisability of using paternal blood. The case which we are presenting substantiates the theory of those workers who are opposed to its use.

In the event that Rh-negative blood were unobtainable, one could conceivably centrifuge maternal Rh-negative blood and administer the cells in normal saline or other compatible serum, since it has been shown by Levine[3] that the antiagglutinin is present only in the serum.

CASE REPORT

J. Y. was born of a second pregnancy, the first having terminated in a normal full-term baby. There was no family history of familial disease including blood dyscrasias. The mother had no complications during this pregnancy, and after a relatively short labor was delivered normally of an 8-pound male infant.

The baby's progress was uneventful during the first four days, except for the existence of mild jaundice which at first was considered physiologic. On the evening of the fifth day after birth, the nurse observed that the baby was very pale and had cyanosis of the finger and toenails. Immediate blood count showed the red cells to be decreased to 1,230,000 with 21 per cent hemoglobin. Blood smears were technically unsatisfactory; however, some erythroblasts were observed.

Physical examination revealed a well-developed and well-nourished newborn infant with marked pallor of the skin and mucous membranes, moderate degree of jaundice of the skin and sclerae, and cyanosis of the nail beds and lips. Respirations were rapid and the cry was weak. No evidence of external hemorrhage was observed. The chest was clear and the heart normal except for increased rate. Neither the liver nor spleen was palpable.

Because of the pallor and respiratory distress, the infant was placed in the Hess bed with oxygen cover and continuous oxygen was given. A transfusion of 80 c.c. of paternal (Rh positive) blood was administered into the anterior fontanel. Two additional transfusions of 75 c.c. each of father's blood were given on succeeding days. Following the first transfusion the count rose to 1.7 with 25 per cent hemoglobin, and after the third, to 2.3 with 47 per cent hemoglobin (Figs. 1 and 2). While such small rises were not considered satisfactory, we did feel that life was being maintained until an Rh-negative donor could be found. The subsequent blood studies taken on the second and third days following the third transfusion showed the counts dropping to 2.0 and 1.9, respectively (Fig. 1).

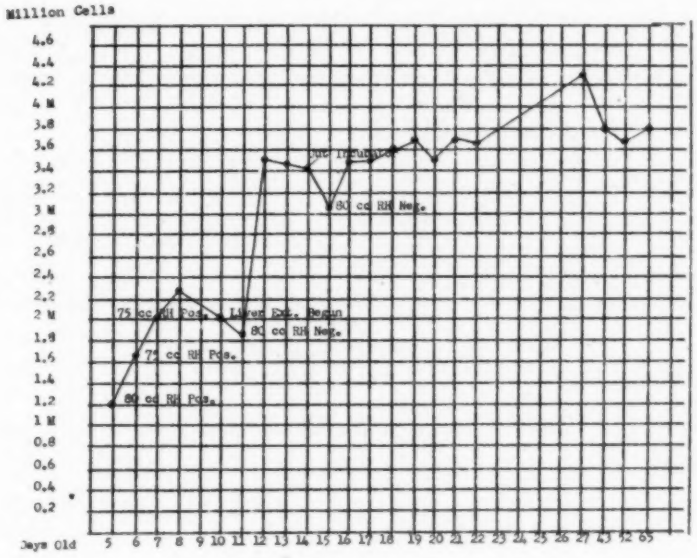

Fig. 1.—Red blood cell response.

On the sixth day following the initial diagnosis, representing the eleventh day of life, an Rh-negative donor was obtained and 80 c.c. of this blood immediately administered. The subsequent red count taken the next day was 3.5 with 57 per cent hemoglobin (Fig. 1). A second similar transfusion was given two days later. Daily blood studies were made during the remainder of the hospital stay, the count being maintained between 3.5 and 3.7 (Fig. 1).

In addition to transfusions and oxygen, 0.3 c.c. of liver extract was given daily by intramuscular injection. The formula consisted of an evaporated milk, water, and Karo mixture.

The baby showed a consistent gain in weight, weighing 8 pounds, 9½ ounces at the time of discharge on the nineteenth day of life (Fig. 3).

The patient has been seen periodically in our outpatient department. He is developing normally and when examined on the ninety-third day of life weighed 13¾ pounds and had a red cell count of 4,000,000.

The laboratory findings showed the father to be Rh positive, the baby's cells to be Rh positive with the serum containing the anti-Rh factor, and the mother's cells Rh negative with antifactor in her serum. The patient's blood smears showed erythroblasts but not as great an increase as expected.

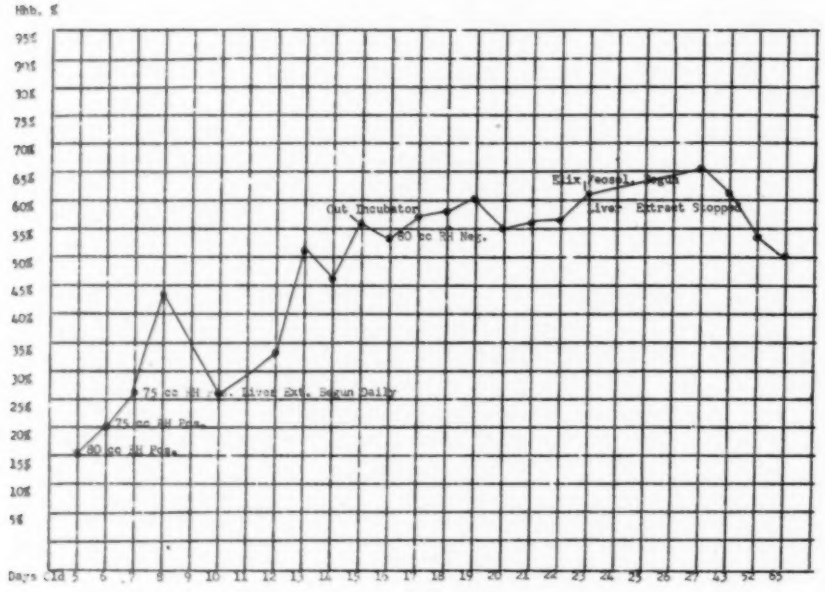

Fig. 2.—Hemoglobin response.

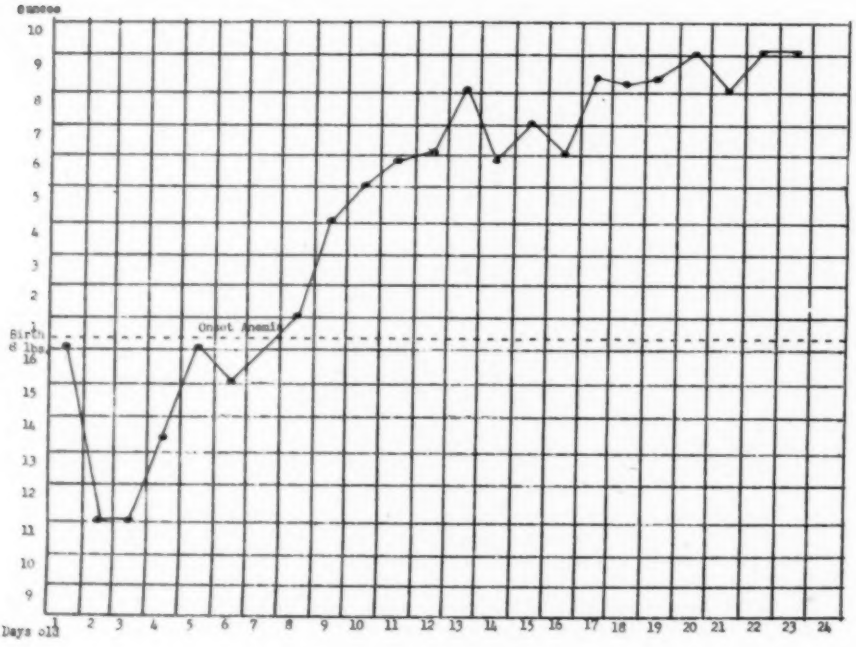

Fig. 3.—Record of weight.

The diagnosis of erythroblastosis was made on the basis of a severe anemia of the newborn infant without evidence of hemorrhage, substantiated by the finding of the combination of an Rh-positive father, Rh-negative mother, and an Rh-positive baby which, according to Levine, Katzin, and Burnham,[3] is diagnostic evidence of the disease.

DISCUSSION

Experience in the treatment of this condition suggests that:

1. Immediate recognition of the clinical entity with institution of appropriate therapy is essential if survival is to be expected. As a result of prompt treatment, the mortality from this disease has decreased from 71 per cent to 14 per cent, according to Javert.[4]

2. Maintenance of external heat and the supplying of oxygen are particularly important during the critical anemic period.

3. Paternal Rh-positive blood is of no therapeutic value, since the donor's cells are destroyed by the antiagglutinin present in the infant's circulation. It is conceivable, however, that in the case here reported, the father's blood originally administered may have been instrumental in maintaining life until Rh-negative blood could be obtained.

4. Since the Rh factor is present only in the cells and the presence of the isoagglutinin is limited to the serum, it is considered safe to use the mother's red cells, after the plasma has been removed and the cells washed twice with sterile saline and resuspended in sufficient saline to make up for lost volume.

5. In considering the case here presented, it is interesting to note that at the time of delivery neither yellow amniotic fluid nor yellow vernix caseosa was noted by the attending obstetrician (H. R. C.). This observation leads us to believe that the development of the isoagglutinin within the mother and its consequent transmittal to the infant occurred quite late in pregnancy and thus accounts for the delayed development of the syndrome. The modus operandi of the breakdown in placental barrier function remains to be determined.

SUMMARY

1. A case of erythroblastosis fetalis characterized by anemia and jaundice is presented.

2. Successful treatment with repeated transfusions of Rh-negative blood and oxygen is reported.

3. A contrast in results when Rh-positive and Rh-negative blood is discussed.

4. A suggestion as to possible therapy, in the absence of Rh-negative blood, is made.

REFERENCES

1. Cutter, Richard D., and Davis, Burt L.: California & West. Med. 56: 17, 1942.
2. Landsteiner, K., and Wiener, A. S.: Proc. Soc. Exper. Biol. & Med. 43: 223, 1940.
3. Levine, P., Katzin, E. M., and Burnham, L.: J. A. M. A. 116: 825, 1941.
4. Javert, T.: Gynéc. & obst. 74: 1, 1942.

BISMUTH SUPPOSITORIES (ANALBIS*) IN THROAT INFECTIONS

BACTERIOLOGY AND PHARMACOLOGY: EFFECTIVENESS, ABSORPTION, EXCRETION, TOXICITY

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IN A previous communication[1] the effective use of bismuth salt of heptadienecarboxylic acid in cocoa butter suppositories was demonstrated in a continuous series of thirty-two cases. These cases included tonsillitis, follicular catarrhal and parenchymatous, nasopharyngitis, and gingivostomatitis. In all cases, the results pointed to this method of treatment as possessing distinct advantages over other methods; these advantages included (1) much greater speed in the recession of symptoms, generally before forty-eight hours, often within twelve hours; (2) more rapid defervescence, generally before seventy-two hours, usually within twenty-four to forty-eight hours; (3) rapid disappearance of objective findings usually within forty-eight hours; (4) greater ease of administration; and (5) complete absence of toxic effects either local or systemic. Cited as controls were previous attacks of similar nature in patients studied, and regardless of the therapy employed, frequently various sulfonamides, the local signs, the symptoms, the elevated temperature, and the constitutional reactions persisted much longer than in those treated with the bismuth suppositories. In all but one of these patients treated, no more than two children size suppositories (0.0225 Gm. metallic bismuth each) were required on succeeding days to produce the results noted.

Still claiming attention, however, are several questions which this communication is intended to clarify further: (1) the urinary picture before, during, and after treatment; (2) the presence or absence of the specific evidences of bismuth toxicity, namely, pigmentation, stomatitis, jaundice, nephritis, dermatitis, or other notable reactions during or after treatment; (3) the presence or absence of evidences of local injury about the site of administration, rectum, anus, lower bowel; (4) the absorption of bismuth as measured by urinary excretion; (5) the margin of safety as measured by the lack of toxicity from the use of more than two suppositories; (6) the incidence and distribution of organisms encountered at the site of the infection; (7) the effectiveness of the treatment as measured against the results obtained by the use of alternate patients treated by other methods as controls.

Forty-one successive patients with tonsillitis, pharyngitis, and gingivostomatitis (twenty-five males, sixteen females, ages ranging from 6 months to 17 years) were included in the study, as they were en-

*The Analbis suppositories were supplied by the G. F. Harvey Co., Saratoga Springs, N. Y.

countered in a pediatric practice within a period of approximately one month, between April 22 and May 25, 1943. Every other patient (Cases 1, 3, 5, etc.) was treated with Analbis (children over 13 years, weighing over 120 pounds, being given adult size suppositories), and the alternate patients (Cases 2, 4, 6, etc.) were treated symptomatically, with the exception of several who received sulfonamides where some special indications seemed to warrant their use (see Table I). The children size suppositories contained 0.0225 Gm. metallic bismuth and the adult size suppositories, 0.045 Gm. Symptomatic treatment in every case consisted of a powder containing acetphenetidin, acetylsalicylic acid, papaverine, and dionin, and a liquid consisting of yellow throat mixture with antipyrin in elixir lactopeptine or elixir vitamin B complex in doses adjusted to the age. Where indicated expectorant or sedative cough mixtures were added. The sulfonamides were administered in doses of 1 gr. per pound per twenty-four-hour period, divided into six doses at four-hour intervals. A throat culture was made in each of the forty-one patients by swabbing the involved area and planting on Löffler's serum, then culturing and, wherever necessary reculturing the organisms for identification. Urinalysis was done on every patient before administration of Analbis and during administration. Request was made for urine specimens one week after the last administration of Analbis, but only a few of the patients complied.

Bismuth determinations were made on all urine obtained (twenty-four-hour specimens) after Analbis administration by the method of Hanzlik and associates.[2] For our bismuth determinations a Klett-Summerson photoelectric colorimeter was standardized, using green filter No. 54, although paper scale color standards are available ranging from 0.25 to 1.2 mg. per 100 c.c. Cole and associates[3] point out that "the ratio of fecal to total bismuth excretion varies widely for different patients" and that the ratio varies widely for the various bismuth preparations used, ranging from 4.8 per cent for bilipisol to 55.8 per cent for thiobismol. Because of the rapid and delicate manner of response of the renal excretion to changes in the bismuth composition of the blood, urinary excretion is considered "a far better index of the blood bismuth level than the total excretion, i.e., fecal and urinary."

Because of the practice of using every patient either as an Analbis-treated case or a control, five patients (Table I), who had unrelated conditions, were included in the series. Of these five patients two (Cases 7 and 39) had scarlet fever, one (Case 29) developed a sore throat and adenitis during the quarantine period following measles and scarlet fever. One patient (Case 15) was being treated for repeated sore throat with fever and developed staphylococcic sepsis and one (Case 33) had an exacerbation of sore throat with adenitis during the course of a rheumatic infection. Only cases of tonsillitis and pharyngitis with adenitis or otitis were included in the figures measuring duration of illness and temperature. Most of the controls had been previously treated symptomatically before I saw them, but the desig-

nation of the duration of the illness and fever were based only on the length of the time that elapsed after they were under my care. However, the five cases mentioned above were useful in gauging any toxic effect resulting from the use of Analbis, because all but one received more than two suppositories and one of the four received eight (Case 15). Other patients received more than two Analbis suppositories

TABLE I

CASE	ORGANISM						TREATMENT	DURATION OF	
	STAPH. ALBUS	STAPH. AUREUS	MICROC. CATARRHALIS	STREP. HEMOLYTICUS	STREP. VIRIDANS	OTHER		ILLNESS (DAYS)	TEMP. (DAYS)
				I. Tonsillitis					
3†	x	x		x			2 Analbis	6	2
4	x	x			x		Symptomatic	10	10
5	x	x	x	x			2 Analbis ad.	1	1
8	x	x		x			Symptomatic	6	6
9‡	x	x	x	x			4 Analbis	1½	1½
11	x	x	x				2 Analbis	2	2
16	x	x	x				Symptomatic	5	5
19	x	x		x			3 Analbis	2	2
20*	x	x		x			Symptomatic	6	6
21†		x					3 Analbis	3	3
22*	x		x				Symptomatic	3	3
23*	x	x	x				2 Analbis	1	1
24	x	x	x				Symptomatic	4	4
26	x					x	Sulfathiazole	5	5
28	x	x	x				Symptomatic	5	5
32	x	x			x		Sulfadiazine	4	4
35	x	x	x		x		2 Analbis	5	5
36			x				Symptomatic	7	4
37†	x	x		x	x	x	3 Analbis ad.	4	4
38	x	x		x			Symptomatic	5	5
40	x		x	x			Symptomatic	6	6
				II. Pharyngitis					
2†		x					Symptomatic	14	8
10	x	x	x		x		Symptomatic	4	4
13	x	x	x			x	3 Analbis	2	2
17	x	x		x		x	3 Analbis	2	2
18†			x	x	x		Symptomatic	9	9
25	x	x			x		2 Analbis	2	2
27‡	x	x	x				4 Analbis	5	2
31	x	x	x		x		2 Analbis ad.	1	1
34	x		x	x			Symptomatic	4	6
				III. Tonsillitis With Otitis					
6	x	x	x				Symptomatic	7	7
30	x	x	x				Sulfadiazine	7	7
				IV. Gingivostomatitis					
1	x	x	x				2 Analbis	4	1½
12		x	x			x	Symptomatic	11	11
14	x	x			x	x	Sulfadiazine	10	8
41	x	x		x			3 Analbis	7	5
				V. Scarlet Fever					
7	x		x	x	x		3 Analbis	3	3
29†§	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.	3 Analbis	3	3
39†	x	x	x	x	x		4 Analbis	5	5
				VI. Tonsillitis With Complicating Rheumatic Fever					
33†	x	x	x		x		2 Analbis	4	
				VII. Tonsillitis With Complicating Sepsis					
15‖	x	x					8 Analbis	5	

Accompanying *adenitis*—*mild, †moderate, ‡marked.

§Adenitis supervening on scarlet fever following measles; throat culture negative.

‖Tonsillitis complicated by gastroenteritis with positive staphylococcus cultures in stools, urine, blood.

(Table I) where effects of more intensive treatment were desired for some specific purpose. All patients given Analbis were watched particularly for the slightest development of any systemic toxic effects of bismuth, namely, pigmentation, stomatitis, jaundice, nephritis, dermatitis, or any other notable reaction. They were also minutely examined proctologically for any other notable evidence of local toxic bismuth effects about the rectum and anus, and the daily stool was watched for any abnormality such as blood. The mean values of bismuth excretion were also calculated (Table II) and the curve of excretion drawn (Fig. 1). The relative incidence of the microorganisms cultured in each case, and their distribution in the various cases is charted in Table I.

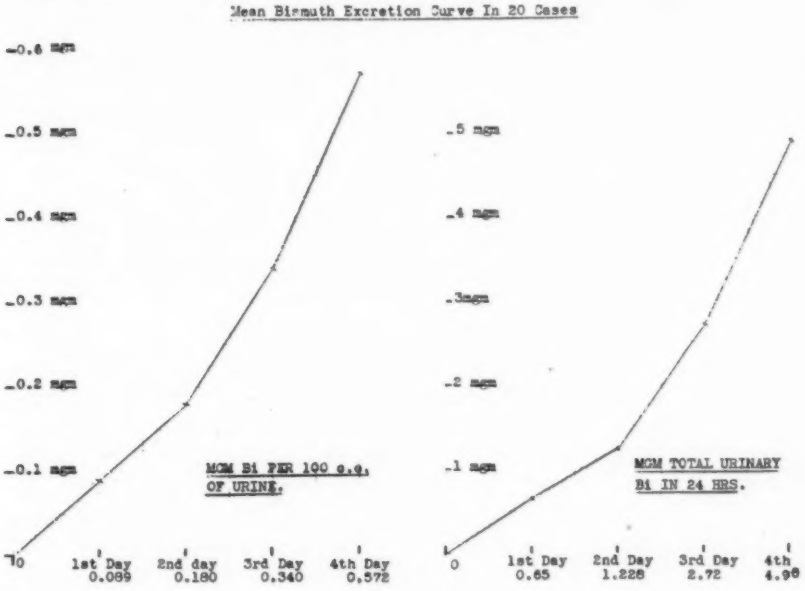

Fig. 1.

1. In every case a casual specimen of urine was obtained at the first visit, before bismuth administration was started, to afford a comparison with subsequent urinalysis made after the use of bismuth. These urinalyses definitely showed no evidence of any harmful effect of bismuth upon the kidneys. In every case studied there was no aggravation of any consequential finding in the casual specimen except Case 39. In this case the casual specimen and the first two specimens after bismuth were negative, but the third and fourth showed a trace of albumin; the severity of the infection accounted for this, because three weeks later examination of a specimen sent to my office was completely negative. In Cases 15, 19, 31, and 41 there were faint traces of albumin in the casual specimens before Analbis was

TABLE II

BISMUTH EXCRETION

CASE	FIRST DAY		SECOND DAY		THIRD DAY		FOURTH DAY	
	(MG./100 C.C.)	(MG./24 HR.)	(MG./100 C.C.)	(MG./24 HR.)	(MG./100 C.C.)	(MG./24 HR.)	(MG./100 C.C.)	(MG./24 HR.)
1	0.040	0.560	0.000	0.000	0.070	0.392		
3	0.000	0.000	0.050	0.255	0.120	0.756		
5	0.000	0.000	0.560	4.200	1.300	12.480		
7	0.020	0.096	0.080	0.768	0.140	1.554	0.570	5.130
9	0.040	0.144	0.080	0.328	0.650	4.680	1.400	12.040
11	0.080	0.384	0.170	0.918	0.560	3.024	0.620	3.348
13	0.860	0.192	0.560	3.416	0.770	4.851	0.660	5.148
15	0.000	0.000	0.000	0.000	0.940	7.990	0.460	3.312
17	0.500	4.050	0.470	3.666	0.660	4.752		
19	0.040	0.216	1.100	6.600	0.090	0.648	0.950	10.260
21	0.000	0.000	0.060	0.720	0.000	0.000	1.080	11.664
23	0.070	0.504						
25	0.045	0.297	0.068	0.448	0.250	2.400		
27	0.008	0.072	0.061	0.604	0.240	2.304	0.440	4.224
29	0.000	0.000	0.001	0.0054	0.054	0.356	0.160	1.152
31	0.009	0.095	0.051	0.581				
33	0.008	0.072	0.008	0.072	0.006	0.050	0.056	0.470
35*								
37	0.000	0.000	0.024	0.230	0.036	0.594	0.085	0.224
39	0.060	0.288	0.054	0.211	0.126	0.680	0.860	4.644
41	0.006	0.062	0.034	0.326	0.120	1.440	0.100	1.020
	(20 cases)		(19 cases)		(18 cases)		(13 cases)	
Total	1.786	13.032	3.431	23.348	6.132	48.951	7.441	63.636
Average	0.089	0.650	0.180	1.228	0.340	2.720	0.572	4.900

*Case 35 was not included in the tabulation because the actual amount of Bismuth given was not determinable on account of loss.

given with negative albumin subsequently during the course of treatment. Acetone and diacetic acid, present in several cases as the result of the infection, and depletion in food intake, cleared up as the patients improved and began to take nourishment. In no case under study were there any casts at any time, any substantial number of red blood cells or white blood cells, or any clinical evidences of nephritis.

2. The other specific evidences of bismuth toxicity: pigmentation, stomatitis, jaundice, dermatitis, or other notable reaction in all cases during or after treatment with Analbis, were completely absent. Actually, as noted in a series of cases previously reported, gingivitis (Case 1) and gingivostomatitis (Case 41) treated with Analbis, rather than being aggravated, cleared up under treatment.

3. The evidences of local injury about the rectum and lower bowel after the use of Analbis were also completely absent on proctologic examination. One youngster weighing 140 pounds (Case 31), who had had an operation performed for fistula in ano two years previous to present illness and who still suffered from a recurring fissure, showed no local injury whatsoever, despite the use of two adult size suppositories 45 mg. each at twenty-four-hour intervals. In Case 15 eight suppositories were used without the slightest evidence of either local or systemic injury in ten days. In no case under study was there any evidence of blood in the stools. In no case was there any discomfort locally following the first minutes after administration.

4. The absorption of bismuth as measured by urinary excretion was very variable for individual cases. According to Cole and associates[3] "most of the bismuth is excreted either by the liver through the bile and feces or even more by the kidneys through the urine. The ratio of fecal to total bismuth excretion varies widely for different patients and necessitates group study to arrive at a mean." Since rectal administration practically precludes the study of fecal excretion, total dependence in our cases for excretion studies had to be placed on urinary excretion. The principles employed by Sollmann and associates[4] in their study have been followed in drawing conclusions as to the urinary excretion of bismuth after treatment with Analbis suppositories. In the excretion studies of Analbis, twenty patients were considered, who received from two to eight children size or adult size Analbis suppositories, or from 45 to 180 mg. of bismuth, the median quantity administered being 77.6 mg. of bismuth. The median daily levels of urinary bismuth excretion (Table II and Fig. 1) were as follows:

First day 0.650 mg. (Average of twenty patients)
Second day 1.228 mg. (Average of nineteen patients)
Third day 2.720 mg. (Average of eighteen patients)
Fourth day 4.900 mg. (Average of thirteen patients)

In calculating averages, it may be noted, that the number of patients decreases progressively from the first to the fourth day, so that by the fourth day only thirteen patients presented urine specimens for bismuth determination, the remaining seven having been discharged at some time prior to the fourth day on account of clinical cure. Analysis of the thirteen patients from whom four daily specimens of urine could be obtained shows that they received a median dose 86.5 mg. of bismuth. Their total daily excretion of bismuth was as follows:

First day	7.526 mg.
Second day	14.198 mg.
Third day	28.171 mg.
Fourth day	63.636 mg.

The average excretion was 2.180 mg. per day per patient, extremes ranging from 0.062 to 12.040 mg. per day per patient. Of a total of 1,125 mg. of bismuth administered to these thirteen patients, 113.351 mg. were excreted during the period of four days, or 10.09 per cent, of the amount administered. Even in syphilis according to Cole and associates[3] "a preparation providing a level of bismuth in the blood stream of such a height as to furnish more or less daily excretion of from 2 to 4 mg. of metallic bismuth should be a potentially valuable antisyphilitic agent." In these individual cases an excretion of from 2 to 4 mg. was noted in nine of the twenty cases treated with Analbis by the third day, and in twelve of the twenty by the fourth day. In all but two of the twenty cases there was an excretion of over 0.5 mg. at some time by the third day (Table II). Cole and associates[3] mention 0.5 mg. urinary bismuth excretion as the level below which therapeutic

effectiveness is not to be expected in syphilis; it is probable that the minimum level is lower in bacterial infections of the oral cavity.

5. The margin of safety as measured by the lack of toxicity from the use of more than two suppositories is well demonstrated in our series of cases. In all cases in which more than two suppositories were used, there was some special reason for their use. Thus two patients (Cases 7 and 39) developed scarlet fever and were given additional suppositories for treatment. The results were as gratifying as the complete absence of local or systemic toxic bismuth effects, despite the tendency of the illness itself to affect the kidneys. One patient (Case 29) had a sore throat, which supervened on adenitis, persisting since an attack of scarlet fever following measles. One patient (Case 35) had an attack of rheumatic fever with an exacerbation of sore throat and adenitis during its course. Another patient (Case 15) had had sulfathiazole at the onset of the illness, three weeks before I started Analbis, with recession of a septic "spiking" temperature after seven days. Then after two days with recurrence of sore throat, fever and diarrhea, again he had been given sulfathiazole plus sulfaguanidine with a recession of temperature after six days. Stool culture at this time showed staphylococcus (predominating). Two days later the sore throat flared up again with adenitis and a temperature of 105° F. The father, who was a chemist and laboratory worker, again insisted on sulfonamides, and sulfadiazine was given with a return to normal in six days. Within thirty-six hours, the patient again had fever up to 105° F. with chills and sore throat, marked malaise, dysphagia, and anorexia, and I started him on Analbis. After four days there was a recession in symptoms, as well as fever, for the first time in over three weeks, and the father insisted on using more suppositories until fluctuations in temperature disappeared for at least three days. Urine culture and blood culture showed pure *Staphylococcus aureus,* and the child was hospitalized. However, defervescence was complete after the eighth suppository, and the child was discharged normal after a week's stay in the hospital. He has since gained weight at a more rapid rate and looks better than ever before. Probably the repeated courses of sulfonamides were effective in producing some bacteriostasis, but positive blood and urine cultures were obtained after their use, while the child was treated with Analbis. The part played by the latter in effecting a cure is an interesting speculation that merits further study. However, the interesting point for our study is that eight suppositories were given in this case with not the slightest reaction either local or general.

6. The incidence and distribution of the organisms encountered at the site of the infection are shown in Table I. Staphylococci (albus, aureus, or citreus as a group) were present in all but three of the forty-one cases, *Staph. aureus* individually in thirty-five cases,

Staphylococcus albus in thirty-three cases and *Staphylococcus citreus* in one case. Streptococci (hemolyticus, viridans, nonhemolyticus) as a group were present in twenty-five cases, *Streptococcus hemolyticus* individually in sixteen cases, *Streptococcus viridans* in twelve cases, and *Streptococcus* non-*hemolyticus* in two cases (Cases 13 and 14). *Micrococcus catarrhalis* was present in twenty-three cases, Vincent's bacillus, in two cases (Cases 12 and 26), and pneumococcus (type XIII), in one case (Case 37). Bacteriologically, infections of the throat seem to be coccal infections involving staphylococci, streptococci, and *M. catarrhalis* in most cases.

7. The effectiveness of Analbis as measured against the results obtained by the use of alternate cases, treated by other means as controls, is well demonstrated in Table I. The average duration of the illness in fourteen patients with tonsillitis and pharyngitis, with varying degrees of adenitis, treated with Analbis was 2.68 days, of fifteen patients treated symptomatically was 6.3 days, of three patients treated with sulfonamides was 5.3 days. The average duration of fever in fourteen patients treated with Analbis was 2.18 days; in fifteen patients treated symptomatically, 5.87 days; in three patients treated with sulfonamides, 5.3 days. The average duration of the illness and fever, respectively, in two patients with gingivostomatitis treated with Analbis was 5.5 and 3.25 days; in one patient treated symptomatically, 11 days and 11 days; and in one patient treated with sulfonamides, 10 days and 8 days. Especially useful for comparison is F. L., who had two severe attacks of gingivostomatitis, listed as Case 14 while under treatment with sulfonamides and as Case 41 when treated with Analbis. In the first instance (Case 14) he was treated with sulfathiazole for ten days before I saw him, and I continued treatment for ten days with sulfadiazine. However, symptoms (painful gums, dysphagia, foul breath) persisted for ten days, and signs (congested, bleeding gums, aphthae, tender, swollen nodes) for eight days. After Analbis (Case 41) the symptoms lasted four days and the signs five days, although the attack was more severe, the fever higher and the invading organisms included *Str. hemolyticus* which was not present in the previous attack. In listing this, only the duration from the time he came under my care (ten days) was tabulated, although actual sulfonamide treatment from the beginning was ten days more. One very important fact, that has been noted, is the complete absence of any aftereffects when Analbis is used, there is no crankiness, weakness, depression or "carry-over" which is so often present when other methods of treatment are employed, especially the sulfonamides. The return to normal is surprisingly complete.

CONCLUSIONS

1. Twenty-one patients with tonsillitis pharyngitis with varying degrees of adenitis, and gingivostomatitis were treated with Analbis sup-

positories containing 0.0225 Gm. (children size) and 0.045 Gm. (adult size) metallic bismuth each, in the form of heptadienecarboxylic acid salt of bismuth.

2. Five of these had unrelated conditions: two had scarlet fever; one, rheumatic fever; one, adenitis following scarlet fever and measles; and one had sepsis. These cases were excluded from certain averages, in this study, that were not pertinent.

3. Twenty alternate patients were treated as controls, seventeen of the twenty symptomatically, the remaining three with sulfonamides.

4. There were no evidences of toxic bismuth effects, either local or systemic, irrespective of the number of suppositories given.

5. There were no evidences of clinical nephritis, nor of any damage of the kidneys on urinalysis in any of the patients treated with Analbis.

6. The mean urinary excretion of bismuth in thirteen patients followed over a period of four days after first administration of Analbis was 2.180 mg. per day per patient. Total urinary excretion in the same thirteen patients over a period of four days amounted to 10.09 per cent of the total amount of bismuth administered.

7. The organisms encountered in stomal infections were cocci in forty cases; staphylococci as a group in thirty-eight cases (albus thirty-five cases, aureus, thirty-three cases, and citreus, one case), streptococci as a group in twenty-five cases, hemolyticus, sixteen cases, viridans, twelve cases and non-hemolyticus, two cases), micrococcus catarrhalis in twenty-three cases; Vincent's bacillus in two cases; pneumococcus type XIII in one case.

8. Treatment with Analbis was more effective than symptomatic treatment.

9. Recovery was effected in cases of tonsillitis and pharyngitis in 2.68 days in fourteen patients treated with Analbis as against 6.3 days in fifteen patients treated symptomatically and 5.3 days in three cases treated with sulfonamides.

10. Recession of temperature to normal in the fourteen patients treated with Analbis occurred in 2.18 days, in fifteen patients treated symptomatically in 5.87 days, and in three patients treated with sulfonamides in 5.3 days.

11. In four patients with gingivostomatitis treated in this series Analbis medication showed advantages over other forms of treatment comparable to those obtained in tonsillitis and pharyngitis.

12. The average number of Analbis suppositories used in twenty cases was 2.70.

REFERENCES

1. Silber, S.: J. PEDIAT. 23: 59, 1943.
2. Hanzlik, P. O., Lehman, A. J., Richardson, A. P., and van Winkle, W., Jr.: Arch. Dermat. & Syph. 36: 725, 1937.
3. Cole, H. N., Sollmann, T., Henderson, K. et al.: Am. J. Syph., Gonor. & Ven. Dis. 25: 143, 1939.
4. Sollmann, T., Cole, H., and Henderson, K.: Arch. Dermat. & Syph. 37: 994, 1938.

OBSTRUCTIVE EMPHYSEMA IN INFANCY

Due to Tuberculous Mediastinal Glands
Report of a Case

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OBSTRUCTIVE emphysema due to tuberculous mediastinal glands is comparatively rare. The status of the condition has been presented by Meneghello and Smith,[1] Spivek,[2] and Barsby.[3] The following case is one of the youngest patients to be reported.

CASE REPORT

Baby D. H. (68402) was first seen on May 14, 1943, at the age of 4½ months with a history of having had difficulty in breathing for the previous three or four days. Before that time he had been in good health and on adequate feedings. The mother, father, and three siblings were said to be in good health.

On examination he was an acutely ill infant whose nutrition was fairly good. The rectal temperature was 99.6° F. Respirations were extremely labored and rapid with supraclavicular bulging on expiration and deep retractions on inspiration. Percussion note was resonant throughout and somewhat hyperresonant over the left chest. Respiratory excursion was poor bilaterally. The breath sounds were short, more markedly so on the left than on the right. The heart was rapid in rate. The tones were of fairly good quality. The abdomen was not distended. The liver and spleen were not palpable. The remainder of the physical examination was essentially normal. The baby was slightly cyanotic.

X-ray examination of the chest taken immediately showed obstructive emphysema of the left lung (Fig. 1). The x-ray report by Dr. Charles Heilman was as follows: "Obstructive emphysema on the left involving the entire lung. The mediastinum was shifted to the right, and there was compression of the right upper lung field. Secondary inflammatory changes were found in the perihilar region of the left lung. There was no opaque foreign body or other obstructing lesion of the left main bronchus."

Bronchoscopy was performed by Dr. George C. Foster. Using both a 3½ mm. and 4 mm. bronchoscope, he found changes of external compression of the left main bronchus. No foreign body was noted. The baby withstood the procedure well.

The baby took feedings poorly. He was slightly cyanotic during the night. The following day the temperature began to rise. The breathing became more labored and obstructed. A little over twenty-four hours after admission tracheotomy was performed by Dr. G. A. Larson, which gave some temporary relief to the breathing; however, after a

From the Fargo Clinic.

short respite the condition continued to get worse, the temperature going steadily up to a peak of 105.4° F. rectally. There was no response to parenteral fluids and sulfonamide therapy. The baby expired the second day after admission.

Autopsy was performed by Dr. W. A. Stafne. His findings in the chest were as follows: "The essential pathological findings were confined to the thorax. There was no free fluid in either pleural cavity. There was considerable emphysema in the anterior mediastinum, evidently from the tracheotomy recently done. There were numerous large lymph glands in the tracheobronchial area which had a firm consistency and whitish appearance on cut section. The left upper lobe was light pink in color with considerable increased crepitation. The lower left lobe was reddish pink in color and over its latero-anterior aspect was a firm dark red nodule measuring 2 cm. in diameter. On cut section this nodule contained a yellow purulent material. The large bronchi were traced down through both lobes, one of which appeared to terminate in this nodule, but no evidence of any foreign body was demonstrable." The remainder of the organs showed no gross changes.

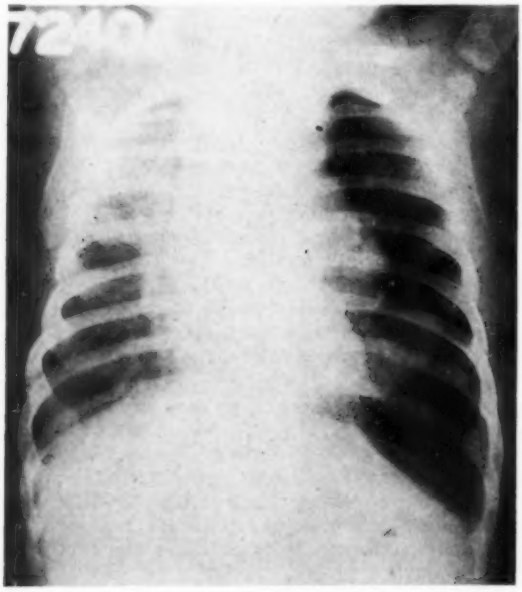

Fig. 1.—Obstructive emphysema, left lung, due to tuberculous glands.

Following the death of the baby the other members of the family had x-ray pictures taken of their chests, which were all normal; however, it was learned that the baby had been exposed to an aunt with active tuberculosis.

DISCUSSION

Obstructive emphysema from tuberculosis may result from simple external compression on the bronchi by enlarged mediastinal glands. A

second way in which obstruction may occur is by ulceration of such a process through the bronchial wall and rupture into the lumen. A mural mass of tuberculous granulation tissue may form on the bronchial wall. A later result may be a cicatricial stenosis of the bronchus. There may be additional nontuberculous factors such as excessive tracheobronchial secretion accumulating below the obstruction; nonspecific infections may play some part in the total process. The condition is more common in infants than in older children or adults because of the greater compressibility of the bronchi during that age period. The mortality in early infancy is almost uniformly bad, but in older infants or young children survival is the rule.

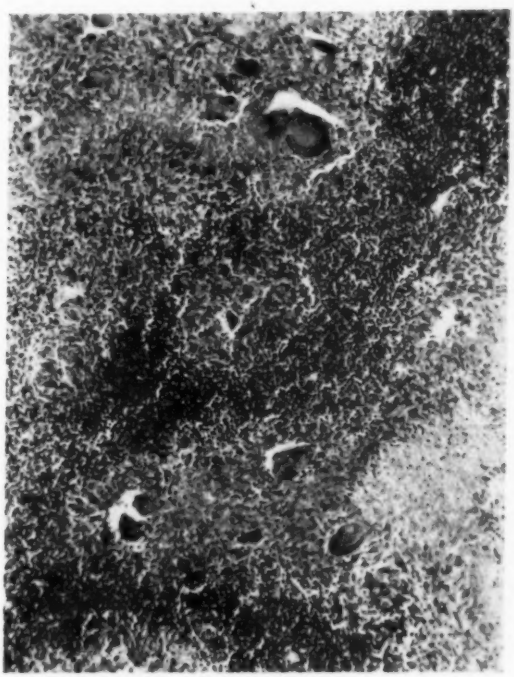

Fig. 2.—Tuberculosis of tracheobronchial lymph nodes.

The mechanism of obstructive emphysema is explained by Jackson and Jackson[4]; the bronchial tubes are larger during inspiration than expiration, and a partial obstruction will allow air to enter the lung but not to leave it. A complete obstruction, on the other hand, results in atelectasis instead of emphysema. Bronchoscopy is recommended in all such cases of bronchial obstruction, not only to rule out foreign body but to remove any mural mass or tenacious secretions that may be present. Otherwise conservative treatment is advised.

SUMMARY

A case of obstructive emphysema of the left lung is reported in a 4½-month-old infant. The obstruction was caused by external compression of the left main bronchus by tubercuious tracheobronchial lymph glands. Bronchoscopy was performed. The infant died. Postmortem examination confirmed the diagnosis.

REFERENCES

1. Meneghello, J., and Smith, C. A.: J. PEDIAT. 22: 265, 1943.
2. Spivek, M. L.: Am. J. Dis. Child. 51: 69, 1936.
3. Barsby, B.: Lancet 1: 627, 1941.
4. Jackson, C., and Jackson, C. L., in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., 1942, W. F. Prior Co., Inc., vol. 2, ch. 50, 55, 56.

STUDIES OF THE NUTRITIONAL STATE OF CHILDREN IN UNOCCUPIED FRANCE IN THE FALL OF 1942

A Preliminary Report

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DURING the fall of 1942 I organized studies of the nutritional state of children in Unoccupied France in connection with the program of the American Red Cross for the distribution of milk to children within certain age groups which its previous investigations, confirmed by competent authorities, had indicated to be in the greatest need of supplemental feedings.* Arrangements were made with members of the faculties of the medical schools of Lyons, Clermont-Ferrand, and Montpellier and with the Institut de Recherches d'Hygiène in Marseilles to carry out a set of identical examinations during the months of November and December on small groups of children who were to receive milk in schools in these cities. Doctors Mouriquand, Rohmer, Hedon, and Kuhlmann, outstanding leaders in the field of nutrition research in France, agreed to direct and supervise the examinations in these cities in the order named and gave the fullest cooperation during the period of organization when many obstacles had to be overcome with speed and energy. I am convinced that they and their staffs of assistants continued their interest after my departure and gave the careful personal attention necessary to assure that the program was carried through with as great technical precision and in as satisfactory a manner in other respects as conditions permitted.

The examination planned for each child included clinical observations, body measurements, and the taking of x-ray films and blood samples. The studies of the latter included determination of hemoglobin concentration and red cell count as well as several biochemical assays. This made the total examination lengthy and called for a considerable amount of the time of the personnel who volunteered to participate, as well as for many laboratory facilities. However, the items included in each category were restricted in so far as possible to important and well-established procedures and the number of children to be examined at each center was limited to a figure acceptable to the local group and,

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This manuscript was prepared by Dr. Stuart, Medical Advisor to the American Red Cross in France, with the Official American Group in Detention, Baden-Baden, Germany.

*Briefly, the American Red Cross general milk program called for the giving of a daily supplement of 125 Gm. of evaporated milk, equivalent to 250 Gm. of whole milk, to children up to 14 years of age and to expectant and nursing mothers, with emphasis, in respect to children, on the age groups of 10 to 14 years and 6 months to 3 years.

except in Marseilles, did not exceed 100 at any one center. In addition to the routine observations made on all the children, certain determinations were made on small groups at single centers, owing to the special interests and opportunities of the local staffs. The principal group studied in each instance was composed of children between the ages of 10½ and 11½ years, but in certain places groups of children of other ages were also examined.

The distribution of milk to these children was to be started immediately after the first examinations had been completed. It was planned that identical examinations be carried out on the same children periodically during the continuance of the supplemental feedings.

After numerous conferences with the people who were to carry out or be responsible for these examinations, a record form was constructed to be used on all the groups, and careful instructions as to its use were prepared and explained to the examining personnel. The data were set up on the examination form in a manner which required only the checking of a code number to indicate the appropriate interpretation of any item and allowed for direct transfer to punch cards. It was hoped that by this means the information obtained would be as precise and comparable as it could be made with a considerable number of people participating in collecting it, and that its recording and compilation would be put on the most efficient possible basis.

I visited the centers where these examinations were being started early in November and observed the first to be carried out. On my departure for Lourdes, France, on November 11, 1942, I left the program under the general supervision of Dr. Daniel Kuhlmann, Director of the Nutrition Section of the Institut in Marseilles. I had been closely associated with Dr. Kuhlmann in studies of nutrition which were conducted under the auspices of the Health Commission of the Rockefeller Foundation in Marseilles during 1941 as well as with the organization of this American Red Cross program during September and October, 1942.

The following report represents studies of preliminary data received in Lourdes late in 1942, consisting of records and the x-ray films of 134 children, especially of 35 girls and 53 boys in the 11-year age group, examined by Kuhlmann and his collaborators. The results of the laboratory determinations made on the blood samples from these children were never received, and the clinical examinations revealed so few and diverse abnormal findings that a discussion of them from such a small group is not justified. This report deals, therefore, principally with body measurements and with certain aspects of roentgenologic findings of 11-year-old children studied in Marseilles. I received records from Dr. Hedon in Montpellier, just prior to my departure for Baden-Baden, Germany, but unfortunately they had to be returned without analysis and compilation of results.

MEASUREMENTS

The measurements taken directly on this group of children were "weight," "height," "chest circumference," and "pelvic breadth." These were supplemented with measurements taken on x-ray films of the leg area, described as "length of tibia," "breadth of calf," "breadth of tibia," "breadth of muscle" and "breadth of skin and subcutaneous tissue."

The techniques used in obtaining the direct body measurements were the same as described in a previous publication[1] based on earlier studies at the same institute in Marseilles. Means have been derived for these measurements from the data received at Lourdes and have been compared with means obtained from measurements of school children in Iowa City as reported by Meredith[2] and by Boynton.[3] These means are presented in Table I together with the percentage deviations of the former from those of the Iowa series.

TABLE I

BODY MEASUREMENTS OF ELEVEN-YEAR-OLD CHILDREN IN MARSEILLES (1942) WITH NORMS FROM IOWA AND PERCENTAGE DEVIATIONS FROM THESE NORMS

MEASUREMENT	BOYS			GIRLS		
	MARSEILLES	IOWA	DEVIATION (%)	MARSEILLES	IOWA	DEVIATION (%)
Weight	29.5	34.3	−14.0	29.8	34.4	−13.4
Height	132.5	143.0	−7.3	134.7	143.6	−6.2
Chest circumference	64.6	64.9	−0.5	62.8	65.0	−3.4
Pelvic breadth	21.9	22.7	−3.5	22.6	22.4	+0.9

The measurements obtained from roentgenograms of the leg area of these children, taken according to a standard procedure described by Stuart and Shaw[4] and extended by Stuart and Hill,[5] have been compared with measurements of normal American children obtained in Boston. Since the norms from these sources do not extend beyond the 10-year age group, the figures used for comparison in this instance have been calculated by adding to the means for 10 years the increments of the means between 9 and 10 years. Although this incorrectly assumes equal increments in each of the two years, it gives values which may be assumed to be close to those which would have been obtained from 11-year-old children in Boston. It is unfortunate that the group studied in Marseilles and elsewhere in France could not have been selected from the 10-year-old group, especially as norms for this age are available from studies by the same techniques in Marseilles in 1941. The reason for the selection of older children in 1942 was that the American Red Cross at that time was not planning to give milk to the children of the 10-year-old age group in the cities where these studies were to be made.

The means for the measurements obtained from roentgenograms are presented in Table II, together with the norms for the Boston group and

TABLE II

MEASUREMENTS FROM ROENTGENOGRAMS OF LEG AREA OF ELEVEN-YEAR-OLD CHILDREN IN MARSEILLES (1942) WITH NORMS FROM BOSTON AND PERCENTAGE DEVIATIONS FROM THESE NORMS

MEASUREMENT	BOYS			GIRLS		
	MARSEILLES	BOSTON	DEVIATION (%)	MARSEILLES	BOSTON	DEVIATION (%)
Tibia (length)	26.37	28.15	−6.3	27.06	29.04	−6.8
Calf (breadth)	8.38	8.96	−6.5	8.80	9.05	−2.8
Tibia (breadth)	2.04	2.29	−10.9	1.99	2.11	−5.7
Muscle (breadth)	7.40	7.80	−5.1	7.59	7.62	−0.4
Skin and subcutaneous tissue (breadth)	0.98	1.16	−15.5	1.23	1.43	−14.0

with the values of the percentage deviations of the former from the latter.

A study of Tables I and II shows that with one exception the mean values for all the measurements of the children in Marseilles are smaller than the values obtained from the American group. The one exception is in the case of breadth of pelvis and this for girls only. The differences are seen to be considerably greater in the case of some measurements than others. A previous study of children in Marseilles[1] has shown that they tend to differ in size and in certain features of build from American standards and that to some extent these differences are probably racial in origin. There were, however, indications in the data presented at that time that faulty growth and lack of certain tissues had frequently resulted from prolonged undernutrition and had played their part in producing the smaller mean values for the measurements of the group.

In the present series, the mean values for height and for length of tibia indicate that the French children were on the average about 7 per cent shorter in linear measurements than American children of similar age, but the figures for pelvic breadth and chest circumference indicate that skeletal breadths are more nearly alike in the two groups. On the basis of build alone, therefore, one would expect that body weight would differ by less than 7 per cent, whereas the actual difference is approximately twice this value. Looking to the measurements obtained from roentgenograms of the leg area for a possible explanation of this deficit in weight, it is seen that the greatest discrepancy between test and standard figures is in the amount of subcutaneous tissue, −15.5 per cent for boys and −14.0 per cent for girls. It would appear that the children studied in Marseilles under this American Red Cross program were, in addition to being somewhat smaller (especially shorter) for age than the American children, lacking in fat and other subcutaneous tissues.

During the winter and spring of 1941 a group of 10-year-old school children were studied in Marseilles, as referred to before. The children were not the same individuals as studied in 1942, but they were selected

in much the same way and were measured by the same techniques and in large part by the same staff. No roentgenograms were obtained from the 10-year-old children in 1941 but films were obtained at that time from a group of 6-year-old children. The percentage deviations of the means of all these measurements from the means of the norms for the 6-, 10-, and 11-year-old children in both 1941 and 1942 are presented in Tables III and IV. The values for the measurements themselves are omitted in order to simplify the presentation.

Tables III and IV show that for most measurements 11-year-old children in 1942 were further behind standards than those 6 years old in 1941, but this is again especially true for body weight and breadth of

TABLE III

PERCENTAGE DEVIATIONS OF THE MEANS FROM AGE NORMS FOR IOWA OF BODY MEASUREMENTS OF CHILDREN IN MARSEILLES IN 1941 AND 1942

AGE (YR.)	YEAR	BODY WEIGHT	BODY LENGTH	BODY HEIGHT	CHEST CIRCUM-FERENCE	PELVIC BREADTH
			Boys			
6	1941	−7.2	−6.1	−6.5	0.0	−2.9
10	1941	−13.9	−5.3	−6.0	+0.9	−0.6
11	1942	−14.0	--	−7.3	−0.5	−3.4
			Girls			
6	1941	−11.5	−6.3	−6.0	−3.2	−0.4
10	1941	−14.4	−7.7	−7.4	−4.4	−2.3
11	1942	−13.4	--	−6.2	−3.4	+0.9

TABLE IV

PERCENTAGE DEVIATIONS OF THE MEANS FROM AGE NORMS FOR BOSTON OF MEASUREMENTS FROM ROENTGENOGRAMS OF CHILDREN IN MARSEILLES IN 1941 AND 1942

AGE (YR.)	YEAR	LENGTH OF TIBIA	BREADTH OF CALF	BREADTH OF TIBIA	BREADTH OF MUSCLE	BREADTH OF SKIN AND SUBCUTA-NEOUS TISSUE
			Boys			
6	1941	−6.9	−2.0	+2.9	+1.2	−0.9
11	1942	−6.3	−6.5	−10.9	−5.1	−15.5
			Girls			
6	1941	−9.1	−2.8	0.0	−1.3	−8.2
11	1942	−6.8	−2.8	−5.7	−0.4	−14.0

skin and subcutaneous tissue. These differences, however, are more probably attributable to age than to year, since there was a similar difference in weight between children of 6 and 10 years in 1941. It appears that the older children were at all times more lacking in subcutaneous tissue than the younger. From a study of these Tables, it is not possible to draw any conclusions as to changes in the state of nutrition of children in Marseilles between 1941 and 1942, even though the diet is known to have been universally and continually well below generally accepted standards from many points of view during this period.

OSSEOUS DEVELOPMENT

In view of the age of the children studied it is not surprising that no evidences of active rickets or scurvy were found in the x-ray films taken in this series. A few films showed very faulty mineralization of bones and still more showed heavy or numerous lines of interrupted growth, but on the whole the series was not conspicuous in these respects.

Roentgenograms of the hand and wrist of the 11-year-old children, taken in Marseilles during November and December, 1942, were read while I was in detention at Lourdes, France. To each satisfactory film an "osseous age" was assigned, using as standards of reference the norms for age presented by Todd.[6] The average retardation of French children, according to these standards and as I interpreted them, was approximately one year in the case of both sexes. As there were only 22 boys and 41 girls of this age on whom satisfactory films were available, the distribution of the ages of the individuals is not given, but the oldest osseous age assigned was 11 years, 3 months and the youngest, 7 years, 9 months. Thus no child was assigned an osseous age above the upper limit of the group in chronologic age (11½ years) whereas more than one-half were considered less mature in bone development in the hand than average for the lower limit of the range in chronologic age (10½ years). This finding of moderate retardation in osseous development among children in Marseilles, when compared with American standards, is in accord with previous findings.[1]

Each child in this series has been assigned an age for each of several body measurements as well as for osseous development in the hand. The method has been to choose the age for which the norm of the measurement most nearly corresponds to his actual measurement. For this purpose the same American standards were used as in the studies already described. A mean anatomic age for each measurement for the French children has been derived from these individual ages. In Fig. 1 the differences between these anatomic ages and the chronologic age of 11 years are shown graphically. By this method of comparison the French children are shown to be as much behind American standards in measurements as in osseous development and considerably more so in body length. Taking all these features into account they correspond most nearly to the standard children with average age of 9½ or 10 years.

GENERAL ASPECTS OF THE NUTRITION OF CHILDREN IN UNOCCUPIED FRANCE LATE IN 1942

A review of the findings of Kuhlmann and his collaborators at the Institut de Recherches d'Hygiene in Marseilles, interviews with physicians and health officers qualified to speak from knowledge of actual conditions, and observations made during travels in Unoccupied France between Sept. 3 and Nov. 7, 1942, lead me to certain general conclu-

sions regarding the state of nutrition of children prior to the inauguration of the latest program of the American Red Cross for their benefit. These are presented very briefly in the following paragraphs to supplement the meager data which I had in hand before being compelled to discontinue the studies presented in this communication.

There had been a considerable increase in the incidence of diarrhea during the summer of 1942 among infants and young children in Unoccupied France, due principally to a deterioration in the quality as well as a lack in quantity of milk. Young children had in other respects enjoyed customary health and were for the most part in fairly good nutritional state. From 8 years onward, but especially between 12 and 18 years of age, there had been a noticeable increase in the number of children showing evidences of undernutrition.

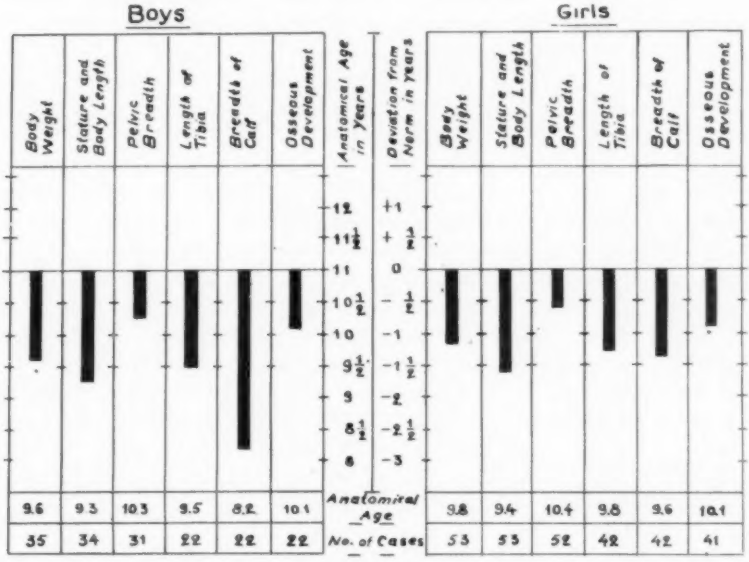

Fig. 1.—Anatomical ages based upon body measurements and osseus development of 11-year-old children in Marseilles in the fall of 1942.

During the summer months of 1942 a considerable proportion of the school children in large cities had been sent to camps such as those organized by the American Red Cross, or to board with families living in localities having more ample stocks of food. Many of these children gained from 2 to 4 kg. during three to five weeks' vacation periods. During these months summer garden products also temporarily improved diets which otherwise had been progressively worsening. In spite of these alleviating factors, the evidences of chronic fatigue, lack of vigor, and inadequate weight for build had gradually become more marked and widespread during the preceding year. However, no im-

portant increase in the incidence or severity of rickets had been noted and other deficiency diseases had remained uncommon. There had been some increase in the incidence of anemia, presumably of the nutritional type, and occasional cases showing protein deficiency had been noted. The blood levels of vitamins A and C had been continually low in samples on which tests had been made from time to time at research centers.

Dietary surveys left no doubt but that the majority of children were taking diets which were very inadequate in total calories and the responses of listlessness and inactivity had been noted by many observers. Diets were for the most part deficient in protein and especially in the proportion of total protein derived from animal sources. They were also lacking in calcium. The situation in respect to the vitamin content of the diets varied with locations and between seasons, but the probabilities were that the provision of vitamins A, C, and D had been quite generally unsatisfactory.

As a result of these, it may be concluded that a state of general moderate to marked undernutrition was widespread in Unoccupied France in the fall of 1942, at least among children over 10 years of age. There was little evidence, however, that this undernutrition had generally reached a stage in which health had yet been profoundly affected, life, endangered, or development, more than moderately retarded. Under these circumstances it was felt that the supplement of 250 Gm. of milk daily which the American Red Cross was planning to give in most instances to children between 10 and 14 years of age would be most helpful. It was not sufficient to meet all the inadequacies in their diets and failed by a wide margin to correct the deficiency in calories for the older children, but it would serve as a valuable protection against the more serious consequences of the food situation which then existed.

REFERENCES

1. Stuart, H. C., and Kuhlmann, D.: J. PEDIAT. 20: 424, 1942.
2. Meredith, H. V.: Studies in Child Welfare, No. 11, University of Iowa Studies, 1935.
3. Boynton, B.: Studies in Child Welfare, No. 12, University of Iowa Studies, 1936.
4. Stuart, H. C., Hill, P., and Shaw, C.: Monograph of Society for Research in Child Development, Vol. 5, No. 3, Washington, D. C., 1940, National Research Council.
5. Stuart, H. C., and Hill, P.: Child Development 13: 195, 1942.
6. Todd, T. Wingate: Atlas of Skeletal Maturation (Hand), St. Louis, 1937, The C. V. Mosby Co.

American Academy of Pediatrics

Proceedings

TWELFTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

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Round Table Discussion on Skin Diseases in Children

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Cutaneous Avitaminoses

Oliver S. Ormsby, M.D., Chicago

Avitaminosis is due to inadequate utilization of vital substances contained in food. It is usually due to an unbalanced diet in which food containing the necessary vitamins is not consumed. Avitaminosis may occur when the food supply is adequate. A vitamin deficiency in the presence of adequate food supply may be caused by loss of vitamins through the intestinal canal from intractable diarrhea, through inability of the intestinal canal to absorb normally the essential dietary constituents, through lack of a bodily factor required to convert vitamins into a usable form, to a high individual vitamin requirement, or to the inhibition, by infection, of the functions of vitamins (Rhoads).

The chief vitamin deficiency diseases are pellagra, beriberi, scurvy, and rickets. The cutaneous avitaminoses characterized by follicular hyperkeratosis include Darier's disease (keratosis follicularis), pityriasis rubra pilaris and possibly keratosis pilaris, lichen pilaris seu spinulosus (Crocker) and xerosis.

Vitamin A

Vitamin A plays an important part in the metabolism of the epithelium of the skin and mucous membranes. The association of nyctalopia (night blindness), keratomalacia, and follicular hyperkeratosis is a well-recognized syndrome due to vitamin A deficiency. An excellent description of this syndrome was given by Frazier and Hu in a group of patients observed in clinics in China. The age of the patients

ranged from 4 to 31 years. The diet previous to development of symptoms consisted largely of cereals with some white cabbage and salted vegetables. In infants and young children the cutaneous changes were xerotic, while in older children and adults follicular hyperkeratosis was present. The papules were described as being firm conical or hemispherical and pigmented. In addition, horny plugs or spines protruded from the hair follicles. Lowenthal observed the association of night blindness, xerophthalmia, and follicular hyperkeratosis in soldiers in East Africa. In all of these patients the condition cleared up with the use of cod-liver oil. Lehman and Rapaport in this country reported upon a vitamin A deficiency affection occurring in children characterized by horny papules often having broken stumps of hair at the summit projecting from hair follicles. There was diminished perspiration and the clinical picture was that of xeroderma. Photometric studies confirmed the diagnosis. Vitamin A in the dosage of from 100 to 300,000 international units was specific.

The best sources of vitamin A are butter, cream, egg yolk, fish liver oils, and green leafy vegetables.

Keratosis Pilaris.—This disease occurs at any age but is more common at the developmental period. It is characterized by the presence of minute horny plugs or papulelike lesions occupying the pilosebaceous follicles and situated chiefly on the arms and thighs though they may occur on any portion of the cutaneous surface. The papules are pinhead-sized, or slightly larger, grayish, acuminate or convex, sometimes capped by a scale or pierced by a hair. The skin presents a rough nutmeg-grater-like surface.

Etiology: The affection often occurs with ichthyosis and is more active in cold weather. Vitamin A deficiency is now considered of etiologic importance.

Lichen Pilaris seu Spinulosus (Crocker).—This affection occurs almost exclusively in childhood and is characterized by minute papules situated in the pilosebaceous follicles, each having a projecting horny spine. The lesions are usually grouped into patches and occur chiefly on the neck, buttocks, trochanteric regions, abdomen, thighs, popliteal spaces, and extensor aspects of the arms. The face, hands, and feet are commonly spared. The eruption appears in crops and is usually symmetrically disposed. Early the papules are red, but they soon assume the normal hue of the skin. It is interesting to note that this condition occasionally occurs in patients having folliculitis decalvans of the scalp.

Etiology: This has only been conjectured until recently, when it was found to belong probably to the vitamin A deficiencies.

Pityriasis Rubra Pilaris (Devergie) or Lichen Ruber Acuminatus (Kaposi).—This is a keratotic papular disease commonly beginning in the second decade of life but may begin as early as the first year. The characteristic lesion is a keratotic or horny papule situated in a hair follicle. In chlidren the usual picture consists of a palmar and plantar keratoderma with patches of keratotic papules around the knees, on the back, and on the extremities. These patches resemble psoriasis. In addition there is usually a seborrheic dermatitis-like eruption on the face and in the scalp. The keratotic papules occurring on dorsum of the fingers so characteristic of the disease in adults do not occur in children. The disease runs an intractable course and its etiology was entirely unknown until recently, when it was demonstrated that a vitamin A deficiency was concerned in its production. In three cases Brunsting investigated the degree of night blindness by measuring the threshold of dark adaptation. Treatment with vitamin A produced improvement but rather slowly. We have had similar experiences.

Keratosis Follicularis, Darier's Disease.—This disease begins, as a rule, in childhood; in many cases on record it began in infancy. It is characterized by hyperkeratotic lesions involving the pilosebaceous follicles. The early lesions are papules which soon become crust covered and coalesce, producing papillomatous, vegetating, and tumorlike new growths. The eruption often begins about the head and face and

spreads to the extremities, the front of the chest, and the inguinal and genital regions. The crusted lesions are brownish and greasy to the touch and eventually become deep brown or darker in color. On the face, temples, the inside of the concha of the ears, and about the angles of the nose and lips, dark, even blackish, greasy crusts form. The scalp is the seat of an oily seborrhea and the vegetating and papillomatous lesions are found in the axillary and genital region. There is also some palmar and plantar keratoderma. The disease occurs often in several generations of a single family. Darier thought the disease was produced by a psorosperm. Bowen proved these bodies to be cell transformations and not living organisms. Peck and others consider the disease a vitamin A deficiency affection. They suggest an hereditary weakness in vitamin A absorption or in conversion of provitamin A to vitamin A. These authors cured three patients, using 200,000 U. S. P. units per mouth daily.

Vitamin G (B_2) Riboflavin

Sebrell and Butler described a symptom complex due to riboflavin deficiency which included lesions at the angles of the mouth resembling perleche. Macerated linear fissures occurred at the angles of the mouth together with a red scaly inflammation of the vermilion border of the lips which, at times, presented a red, shiny, denuded appearance. There was an associated mild greasy seborrheic dermatitis in the nasolabial folds and inner and outer canthi of the eyes. Occasionally the seborrheic dermatitis involved the ears and other portions of the face. At times a crusted and superficially eroded lesion was present inside the nares with a fissure at the mucocutaneous junction. The tongue presented a magenta color, which contrasts with the bright red tongue of pellagra. Sometimes these lesions had an associated vascularizing keratitis. This produced photophobia, dimness of vision, circumcorneal injection, and burning sensations of the eyeball. Conjunctivitis is simulated and corneal opacities, mydriasis, and iritis occur.

The best sources of riboflavin are milk, eggs, liver, muscle, and yeast. The dosage ranges from 2½ to 50 mg. daily.

The iritis of rosacea now considered a riboflavin deficiency does not occur in children.

Pellagra.—Pellagra in children is quite common in endemic areas. In alcoholic and other nonendemic types of pellagra, children are rarely affected. In endemic areas of the southern states subclinical pellagra frequently occurs in infants. This is cleared up by treating the mothers. In children the general symptoms are not as marked as in adults, and cutaneous manifestations are particularly important here in diagnosis. These children are below normal in weight and height, slow in school, unable to concentrate. They have a poor appetite, suffer with indigestion, are constipated, and have a sore tongue and sore lips. They are cross and fretful and cry easily. Their food is rich in carbohydrates. Naturally when the characteristic dermatitis and glossitis appear, the diagnosis of active pellagra is evident. It is now generally conceded that the disease is an example of multiple avitaminosis, the chief deficiencies being nicotinic acid, thiamine chloride, riboflavin, and vitamin B_6. Goldberger and his associates were able to clear up the symptoms and prevent recurrences by food rich in the above-named vitamins and to produce it with foods lacking these vitamins. Foods rich in pellagra preventive and curative vitamins include much lean meat, turnip greens, tomatoes, green peas, spinach, and cow peas. Goldberger produced the disease with a diet which included wheat flour, corn meal, grits, starch, rice, Irish and sweet potatoes, some green vegetables, fats, sugar, and syrup.

While a dietary deficiency is all important in producing the disease, it cannot be said that other factors not yet demonstrated may enter into the picture. The demonstration by Goldberger and his associates of the part played by diet was an achievement seldom attained in medicine.

Vitamin C

Vitamin C (ascorbic acid) deficiency is represented by scurvy. This condition is readily cleared up and prevented through the free use of juices of citrus fruits and tomatoes which contain much ascorbic acid. Other sources of ascorbic acid are green leafy vegetables and berries.

The general symptoms need not be described here other than to say that the disease is not uncommon in this country and that the lesions in the mouth and the petechial hemorrhages in the skin are characteristic.

Sclerema Neonatorum, Edema Neonatorum, Subcutaneous Fat Necrosis, and Scleroderma in Infants

Oliver S. Ormsby, M.D., Chicago

Much confusion has existed concerning the above-named conditions as to whether or not they were separate entities. Until a few years ago the condition we now know as subcutaneous fat necrosis was considered to be scleroderma of the newborn infant and even recently sclerema neonatorum has been used as a synonym of subcutaneous fat necrosis. We believe they comprise four distinct diseases and will so describe them.

Sclerema Neonatorum (Sclerema Adiposum).—This disease usually occurs in undernourished, debilitated, and premature infants. It begins suddenly about the third or fourth day or later up to several weeks. Early changes occur on the lower extremities, usually the calves, and extend upward. It may become generalized, avoiding the palms, soles, and scrotum. The skin becomes shrunken, smooth, whitish or waxy, and cold to the touch. The temperature is usually subnormal. Diarrhea is usually present. The indurated areas are hard and do not pit. Movement is limited or nearly entirely inhibited. The pulse and respiration are slowed and the appearance of a frigid cadaver is simulated. Cystic swellings containing fat and needlelike crystals are recorded. As a rule, the disease ends fatally in a few days.

Etiology: A predisposing cause consists of a reduced olein content of the subcutaneous fat in the newborn infant.

Histology: Stearinlike hardness of the fatty tissue combined with dehydration of the skin and subcutaneous tissue is found. No fluid escapes upon incision.

Edema Neonatorum (Sclerema Edematosum).—This disease begins from the second to the fourth day of life usually in weak and premature infants. The early edema is situated on the dorsum of the feet from which situation it extends to the calves, thighs, and mons veneris. It also involves the upper extremities and eyelids. The edema is at times extensive. Early the color may be reddish or it may present a yellowish hue from associated jaundice. The temperature is low (not as low as in sclerema adiposum). The disease is usually fatal within a few days. It differs from subcutaneous fat necrosis in that there are no well-defined plaques. The involved areas pit on pressure and there is an elastic feeling in the skin in some cases.

Histology: There is an intense edema with no specific inflammatory changes. The cause is entirely unknown.

Subcutaneous Fat Necrosis of the Newborn Infant.—This disease occurs in healthy, well-nourished babies. The lesions begin in from two to twenty days after birth as deep-seated indurated areas in the subcutaneous tissue. They vary in size from split pea to hen's egg to large areas covering the greater part of the back and buttocks and are slightly elevated. The color is bluish red early. This gradually clears up before the lesions have softened and disappeared. The surface is smooth and there are no sensations. The skin is indurated and cannot be pinched up between the fingers. The plaques and nodules are well defined and may or may not be movable. Smaller nodules are freely movable. Fluctuation occasionally is present.

The chief areas of involvement are the back, cheeks, arms, thighs, and buttocks. Exempt areas are the palms, soles, axillae, and inner aspect of the thighs. The mucous membranes are rarely if ever invaded. Softening and absorption begins from the fifth to sixth week and is complete in from three to four months. The lesions disappear completely, leaving no trace. A possible slight atrophy was recorded in two cases.

Histology: Necrosis of fat cells occurs and there is an infiltrate of epitheloid and giant cells. Elastin is absent in the center of the infiltration. In the fat cells, which are increased in size and often multinucleated, are numerous needlelike crystals in the form of sheaths or rosettes possibly composed of fatty acids. The infiltration is especially marked at the periphery of fat lobules and consists of lymphocytes, fibroblasts, foreign body giant cells, and occasional eosinophiles. The infiltration occasionally penetrates the interior of the fat lobules. Some giant cells are filled with crystals radiating from the center.

Etiology: Trauma and cold are cited as exciting factors.

Diagnosis: Panniculitis, Weber-Christian disease, as seen in adults, resembles subcutaneous fat necrosis of infants. It differs in that the subcutaneous nodules and plaques terminate after resolution in atrophy. The early lesions are hard, sclerotic, freely movable, irregular masses. With the development of new lesions a constitutional febrile reaction occurs.

An afebrile and a liquefying form has been recorded.

Scleroderma.—Scleroderma in children is rare. All types seen in adults have been recorded in children. The form which suggests an infectious basis has been described by Goodman, Oliver, and others. In this form induration begins about the neck and often follows tonsillitis. The condition becomes generalized and presents the usual picture seen in the edematous form of scleroderma in adults. After several months the induration is absorbed and the skin returns to normal. This is the history of subcutaneous fat necrosis formerly thought to be scleroderma. Time may remove these fairly acute cases from the category of scleroderma.

Mycotic Infections of the Skin

Francis E. Senear, M.D., Chicago

The clinical conception of fungus infections of the skin, particularly as this term applies to ringworm and yeast infections, has undergone great change in recent years. In earlier days when one mentioned cutaneous fungus infections, he probably had in mind trichophytosis capitis, tinea circinata, tinea barbae, tinea cruris, and pityriasis versicolor.

In 1888 Pellizari first reported the presence of fungi in cases of eczematoid dermatitis of the hands. In 1892 Mouktar reported the same finding in cases of dermatitis of the hands and feet. Whitfield in 1908, Castellani in 1910, and Duhring in 1912 made similar observations. It was not until 1916, however, when Ormsby and Mitchell presented a large series of cases before the American Medical Association that widespread recognition of the existence of this type of ringworm infection was attained. Since that time, through increasing recognition and increasing prevalence of the disorder, this type of ringworm infection has become the outstanding example of mycologic cutaneous involvement.

Until recent years, yeast infections of the skin were practically unrecognized and little attention was given to any type of yeast infection except in the case of thrush. Since 1914, however, various cutaneous pictures have been successively recognized as being due to infection with the yeastlike organisms until now the monilial group of infections constitutes a very important phase of dermatology. It is our purpose today to review some of these older and newer types of fungus infections.

Ringworm of the scalp is a relatively common disorder; the condition is largely limited to the preadolescent period since ringworm of the scalp in the adult is exceedingly rare. Trichophytosis capitis is caused by a variety of organisms, generally

recognized as being the microsporon and trichophyton type. The microsporon variety of infection may be of human origin due usually to *Microsporon Audouini* or may be of the animal type due to *Microsporon lanosum*. The first type is much more difficult to cure than is the second, and with the audouini form of infection x-ray epilation is commonly required, while with the lanosum type the use of local treatment usually suffices. The human type of microsporon infection usually gives rise to the so-called gray patch type of infection, there being little inflammatory element. The animal type usually shows a larger number of patches than does the human type and there is usually present a more markedly inflammatory element.

Other cases are due to infection with the trichophyton group of organisms, these being of the endothrix type. They produce a characteristically rebellious form of infection, occurring with many small disseminated lesions with slightly inflammatory reaction. Other organisms in this group tend to produce the black dot type of ringworm infection. In both of these types epilation by means of x-ray treatment is usually required.

Another type of ringworm of the scalp which is usually due to *Trichophyton gypseum ectothrix* is that known as kerion Celsi. In this type the lesions are markedly inflammatory in character, elevated, edematous, leading to the formation of soft boggy masses with exudation of pus from the dilated follicles. In this type the reaction often leads to spontaneous cure within a few months.

Eczematoid Ringworm of the Hands and Feet.—This disorder tends to occur most commonly upon the feet, but the hands are likewise frequently involved and not uncommonly extension to other parts of the body takes place. The most common manifestations are the three clinical varieties known as the intertriginous, vesicular, and hyperkeratotic types. In the first-named variety the patient usually shows a maceration of the epidermis between the toes, although at times there may be vesicles leading to the presence of erosive lesions. In other cases the epidermis does not present a sodden appearance but dry scales may be seen. The condition may limit itself to this type of manifestation for months or years, but in many instances the patient eventually develops the vesicular variety. In this form the lesions occur particularly upon the soles and not infrequently upon the palmar aspects of the hands as well. This manifestation constitutes clinically the picture long designated by the terms pompholyx or dysidrosis. The vesicles tend to occur in groups and the individual lesions are deeply seated, being described as having a boiled sago grain appearance. Within a few days' time the fluid content is absorbed and a brownish spot remains. Eventually the dried roof of the lesion is broken or exfoliated, leaving an inflammatory base surrounded by a collarette of undermined scales. Through coalescence of such lesions, the characteristic eczematoid patches are formed. It is now recognized that the vesicular stage of the disease, which is commonly characterized by a sudden onset, is due to a transmission of the organisms or their toxic products through the blood stream rather than to external transference of the infection.

In some instances the vesicles lead to the production of brownish keratotic buttons and through coalescence and the persistence of such hyperkeratotic lesions, the patient may develop large, dry, scaling patches, this constituting the hyperkeratotic variety of the eruption.

Eczematoid ringworm of the hands and feet typically involves the plantar and palmar surfaces, and if the dorsal aspects of the hands and feet are involved, the first-named areas are usually more intensely affected. In association with eczematoid ringworm infection of the hands and feet, the fungi are not infrequently carried to other parts of the body. A common concomitant finding is the presence of tinea cruris, while involvement of the external genitals, perineum, and anal region is also encountered. As a matter of fact, many cases of pruritus ani, scroti, or vulvae with eczematoid manifestations of these parts are due to this type of infection, and one should never overlook the possibility of such an etiologic

agent in cases of pruritus or eczema of these parts since the prognosis is much better if the fungus etiology is recognized and proper parasiticidal measures used.

A word of caution is necessary because with increasing familiarity with eczematoid ringworm infection, many practitioners have become accustomed to designate almost any type of eczematoid dermatitis of the hands and feet as examples of eczematoid ringworm infection. It should be kept in mind that contact eczema, nummular eczema, streptococcic dermatitis, and continuous acrodermatitis must be considered as diagnostic possibilities in many instances. The usual flexor surface involvement in ringworm infection, the sharp circumscription of the patches, the tendency to central involution with peripheral activity in the patches, and the presence of an overhanging scale at the periphery are important differentiating diagnostic signs found in cases of eczematoid ringworm infection. In many instances, however, demonstration of fungi by direct examination or by cultures is necessary to eliminate these other dermatoses as possibilities.

A very important phase of this type of fungus infection is the recognition of the frequent occurrence of the more widespread types of eruption which are due either to the hematogenous dissemination of the fungi or to their toxic products. These eruptions are grouped under the heading of epidermophytids. As already stated, the vesicular phase of this eruption is generally looked upon as belonging in this group. In many instances, however, the eruptions are more exanthem-like, representing a distinct allergic reaction. They are particularly apt to occur following the institution of therapeutic measures for the localized infection. They may be papular, follicular, or lichenoid and may resemble lichen spinulosus, erythema multiforme, eczema, and other dermatoses.

With regard to the therapy of eczematoid ringworm infection of the hands and feet, some general statement may be made. In the first place, it is obvious that an eruption which has such a great variety of clinical manifestations should not be treated by any single method. In the acute vesicular stages where there is often also a secondary pyogenic infection, it is, as a rule, wise to limit oneself to the use of bland soothing applications. For this purpose wet dressings of aluminum subacetate solution in ½ per cent strength is probably the most uniformly satisfactory application. When secondary infection is present, compresses of potassium permanganate solution in a strength of 1:6000 are likewise valuable. When the acute phases have been overcome, and only then, should one begin to employ the parasiticidal agents. Even here, however, it is well to avoid at the outset the use of too great a concentration of active agents. With Whitfield's ointment, for example, the full strength preparation is often apt to give rise to uncomfortable reactions and to cause acute flare-ups, and a one-half-strength preparation is to be preferred until one is certain that the skin in the individual case will tolerate greater concentration of salicylic acid. There are, of course, many preparations available for the treatment of eczematoid ringworm infection, but the highest proportion of successful results is obtained with the use of salicylic acid preparations, of which Whitfield's ointment is the best known and most widely used, or with the use of iodine preparations. The latter may be employed in the strength of from 2 to 5 per cent of iodine crystals dissolved in benzol or in the following formula:

Tincture of iodine	30.0
Potassium iodide	1.0
Aqua distillata qs ad	100.0

Such solutions are painted on the affected parts once daily. Potassium permanganate solution in 1:4000 strength painted on the intertriginous areas once daily is often a useful treatment to cause drying of the moist and macerated tissues. After this has been accomplished, it is then advisable to resort to the use of one of the more active fungicidal preparations.

Monilial Infections.—As indicated above, a number of conditions which previously were thought to be unrelated have been recognized in the past twenty years as being manifestations of infection of the skin and mucous membranes with organisms of the yeastlike type, and these conditions are now generally grouped under the heading of monilial infections of the skin. The ordinary picture of thrush as seen in infants is too well known to require consideration at this time. There are, however, many cases of monilial infection of the mucous membranes, particularly in adults, which present pictures quite unlike those seen in thrush. Superficial glossitis, hyperemia of the fungiform papillae, localized but sometimes extensive membranous plaques resembling leucoplakia, and the formation of whitish membranous lesions often having linear, stellate, or scroll-like patterns may be seen.

An important type of monilial infection is that which gives rise to redness and maceration of the epidermis and fissuring at the commissures of the mouth. This condition has long been recognized under the name perlèche and for many years was thought to be due to streptococcic infection. In 1929, however, Finnerud, reporting an epidemic of this condition occurring in a large number of children in an orphanage, was able to demonstrate that in these cases the clinical picture was due to infection with the yeastlike organisms. While it cannot be stated that all cases of perlèche are due to this type of infection, a very considerable proportion of such cases do have such an etiologic agent. This condition has likewise long been recognized as a condition which is associated with avitaminosis, and the therapy of perlèche, in addition to the local treatment, commonly requires the use of vitamin B complex.

In the same group of children, Finnerud also noted that there were many instances in which the patients presented noninflammatory, dry, whitish, scaly patches upon the cheeks, constituting the disorder known as impetigo pityroides. He was also able to recover the fungi from these lesions, and it is now recognized that impetigo pityroides is in many instances due to a monilial infection.

Another common type of monilial infection is the intertriginous variety. Patients who present dermatitis in the folds of the body, principally in the submammary region, in the retro-auricular folds, in the folds of pendulous abdomens, in the crural region, and in the anal fold often have such a manifestation as a result of monilial infection. These lesions usually begin with the development of very superficial and tiny vesicles. The vesicles rupture, leaving a little fringe of epidermis at the edge of the lesion. Through coalescence of such lesions large denuded, and sometimes scaling, inflammatory patches are produced, but at the periphery of the patch the characteristic early lesion may usually be found. When these organisms involve the folds of the body, they are prone to produce a considerable degree of maceration, and while clinically it is often impossible to distinguish between the lesions of ringworm and monilial infections of the folds of the body, the tendency to maceration is usually more intense with the latter type.

An interesting form of monilial infection is that known as erosio interdigitalis saccharomycetica. This disorder is seen upon the hands, usually affecting only one hand, most often involving the web between the middle and ring fingers. Occasionally the disorder may be symmetrical and bilateral and at times more than one interspace is involved on the same hand. The disorder is particularly common among Jewish people and is much more frequently seen in women than in men. It occurs particularly in those individuals who have to immerse their hands in water or other liquids frequently. Clinically the lesion is very characteristic, consisting of a large, patchy, bright red-appearing area surrounded with a collarette or scales. In some instances the erosive base is covered with a layer of sodden epidermis. In the typical picture the border of the lesion is characterized by a collarette of scale.

These organisms not infrequently invade the paronychium, thus giving rise to monilial paronychia. This disorder is likewise seen particularly in laundresses, dish washers, soda fountain attendants, salad makers, fruit packers, and in those whose

hands are frequently immersed in solutions. The condition is usually seen about the posterior nail fold where it produces a characteristic swelling. This swelling is roll-like in appearance and is often described as a bolster roll or a sausage roll. The condition is inflammatory, and by pressure upon the swollen posterior nail fold, one is often able to cause the extrusion of a small amount of pus. The lateral nail folds and nail plate may be secondarily infected.

The monilial organisms may produce both in children and in adults a variety of genital lesions, among which is a vaginitis characterized by a picture resembling that of oral thrush. In such cases the vulvae are apt to be affected and the changes here may appear as vesicopustular, ulcerative, pseudoleucoplakic, or eczematoid lesions or by pruritus with little or no cutaneous manifestations. It should also be emphasized here, as in the case of ringworm infection, that many cases of eczema or pruritus of the vulvae, scrotum, perineum, and perianal region are due to monilial infection. The same statement with regard to betterment of the prognosis through detection of the fungus causation is applicable here.

On occasion, instances of systemic and generalized cutaneous infection with the monilial organisms have been reported, sometimes leading to a fatal termination. Rockwood and Greenwood, Downing and Hazard, and Schultz and others have reported and described cases of this extremely chronic type of infection.

Allergic reactions, comparable to those discussed as epidermophytids, are seen in association with monilial infections. In cases of infection with the yeastlike organisms, such lesions are disseminated moniliids. The latter type of eruption usually manifests itself in the form of small, grouped intra-epidermal vesicles occurring upon the extremities. Eczematoid eruptions, pompholyx-like eruptions, and others are likewise seen as manifestations of allergic reactions to localized monilial infections.

DISCUSSION

DR. C. S. BAUMAN, WATERVILLE, MAINE.—How about the phenol and camphor treatment in ringworm?

DR. SENEAR.—The phenol and camphor treatment is not particularly new, but much attention has been given to the method since the appearance of the article by deKruif in *The Reader's Digest*. As was pointed out at that time, the preparation is not safe for use in the presence of water or serous discharges and many dermatologists have seen patients who have been severely injured by the use of this application. As was to be expected, since lay people are prone to diagnose many types of lesions having no relationship to fungus infection as ringworm, the preparation has been used in a variety of other dermatoses, and not infrequently this has led to serious and, in some instances, disfiguring phenol burns. While I have had no extensive experience with the use of the phenol-camphor preparation, I have the distinct impression that one cannot be optimistic about the results to be obtained. Certainly the preparation is not one which should be made available for use by the laity without proper medical control.

DR. H. L. ELIAS, ROCKVILLE CENTRE, N. Y.—Discuss the treatment of monilia.

DR. SENEAR.—The treatment of monilial infection has to be considered in much the same way as the treatment of eczematoid ringworm infections. Generally speaking, the best results are obtained with the use of dyes, and of these a 1 per cent solution of genitan violet is most widely employed. Pyoktanin and blue, brilliant green, and other dyes may also be used. As is the case with ringworm infection, iodine preparations are likewise effective in the treatment of this disorder. The salicylic acid preparations, such as the Whitfield ointment used in eczematoid ringworm infection, are likewise of value, but when they are to be used in the folds of the body, one must be careful to avoid irritation from too great a concentration of

the salicylic acid. Just as in the acute phases of ringworm infection, so here it is often necessary to treat the acute dermatitis before resorting to the more active agents. Soothing applications of the shake type or wet dressings of aluminum subacetate solution or bland pastes may be needed at the outset of treatment. It is well to keep in mind that patients occasionally suffering with monilial infections have diabetes and that the treatment of an underlying diabetes when present is an essential part of the treatment of the cutaneous infection. In recent years it is likewise well recognized that in many instances patients suffering with monilial infection will not recover unless the topical therapy is supplemented by vitamin therapy. The use of B complex or, at times, parenteral administration of liver extract may be of great service in cases of this type.

DR. T. P. SALTIEL, CHICAGO.—Has sulfathiazole any place in therapy of ringworm?

CHAIRMAN ORMSBY.—Sulfathiazole has been used extensively and with success in pyogenic infections, but I believe it is of little or no value in mycotic infections.

DR. JOHANNA FELDMAN, CHICAGO.—Is iodine still useful for treating ringworm of the body?

CHAIRMAN ORMSBY.—Iodine in some forms is very valuable in the treatment of ringworm of the glabrous skin.

DR. ELI RUBENSTEIN, BAYONNE, N. J.—Is there anything better than gentian violet in treating tinea cruris?

CHAIRMAN ORMSBY.—Gentian violet is more valuable in the treatment of yeast infections than it is in epidermophyton or trichophyton infections. We employ soakings with a 1:2000 solution of potassium permanganate followed by the local application of a 50 per cent Whitfield ointment or a 5 per cent chrysarobin ointment. These ointments should not be used longer than five days because of possible reactions.

DR. H. H. PERLMAN, PHILADELPHIA.—Can epidermophytosis of the feet be prevented by Whitfield's ointment?

CHAIRMAN ORMSBY.—Whitfield's ointment is valuable as a preventive only when latent microorganisms are present in calluses or beneath or around the nail plates. Soaking the feet with a 1 per cent solution of sodium hypochlorite is a valuable preventive.

DR. J. A. JONES, SWATHMORE, PA.—What solutions should be used around swimming pools?

CHAIRMAN ORMSBY.—The preventive measures used around swimming pools and in gymnasia consist in using a 1 per cent solution of sodium hypochlorite in pans in which the feet are immersed before and after the shower.

Comment

THE AMERICAN ACADEMY OF PEDIATRICS AND THE CHILDREN'S BUREAU

THE "statement" of the Executive Board of the Academy and the explanatory editorial in the July issue concerning the relationship between the Academy and the Children's Bureau has brought forth considerable comment. Most of this has been in agreement with, or has expressed approval of, the action of the Executive Board.

The closing date for publication of this number has been delayed in order to publish the following correspondence. The editors feel that every opportunity should be given to those who wish to express views differing with the action of the Board. At the annual meeting of the Academy in St. Louis in November an entire evening has been set aside for a full discussion of the EMIC Program, and a later afternoon business session at which the Academy membership may take any action the majority present may decide.

A Letter to the Editors

The action of the Executive Board of the American Academy of Pediatrics in advising withdrawal of Academy support of the United States Children's Bureau, as reported in the July number of THE JOURNAL OF PEDIATRICS, seems to me most ill-advised. In view of the fact that the special committee appointed by the Academy made a favorable report on the administration of the Emergency Maternity and Infant Care program, the action of the Executive Board on that basis is not warranted. Furthermore, in the Executive Board action on and preamble to this report and in the Editorial there are evidences of fears and dissentions which bode ill for maternal and child welfare and for pediatrics in America.

Since its establishment in 1912, the Children's Bureau has worked valiantly with pediatricians, obstetricians, and other workers in the struggle for better care for children and their mothers, has cooperated with and stimulated forward-looking physicians, inaugurated and aided relevant investigative work and conducted far-flung and comprehensive educational programs and demonstrations. The educational features of the activities of the Children's Bureau have reached all sorts and conditions of our population in vast numbers as well as our professional groups, medical and social.

It has been pointed out countless times by pediatricians as well as by workers in the fields of the social sciences that a federal children's bu-

reau should not stand for health alone but rather for an integration of all aspects of child life. This point of view our Children's Bureau has consistently, vigorously, and successfully held as a fundamental policy. Having this concept of its function, it has been fortunate from many points of view that the Bureau has been located as a closely affiliated but almost autonomous unit in the Department of Labor where many of the socioeconomic problems of maternal and child life are brought for governmental and administrative action. The White House Conference of 1930 emphasized the importance of considering the child as a unit, namely, that his physical and mental development and his social and economic environment should be part and parcel of unified and continuous consideration from prenatal life through adolescence. The Children's Bureau as at present organized represents in its every activity this integration. Dispersion of governmental responsibilities so far as the different aspects of child life are involved would constitute a step backboard from the high point reached in our present concept of child welfare. The essential point is, in my opinion, that an integrated approach to the varied aspects of maternal and child welfare be preserved wherever in the Government a Children's Bureau exists.

The multifarious activities of the Children's Bureau in the promotion of maternal and child welfare have been carried out for thirty-two years without scandal or political intrigue; the programs authorized by Congress have achieved fruition with standards ever high and record unsullied. For this pediatricians and obstetricians should be proud and deeply grateful; they have had an ever-growing share in the Bureau's work and achievements.

For each of its special programs the Bureau has had a definite mandate from Congress which in turn was responsive to certain needs of the people. These needs were brought to the attention of the Government by individuals and by organized groups of widely diversified character. But there was a unifying bond bringing them together to ask assistance from their elected representatives, namely, a common interest in the welfare of mothers and children. This is the prime business of the Children's Bureau; and the public and Congress alike, recognizing this dominating function, have placed trust and responsibility in accord therewith.

These congressional mandates are available to all who desire to follow the legislative course of Children's Bureau activities: the organic act establishing the Bureau, 1912; Sheppard-Towner Act, 1921; Social Security Act, Title V part 1, 1935; Fair Labor Standards Act, 1938; Emergency Maternity and Infant Care—Joint Resolution of Congress, 1943; Federal Security Appropriation Act, 1944.

To the writer it seems a tragedy that by action of the Executive Board of the American Academy of Pediatrics the public may conceive of pediatricians as more interested in preserving certain professional mores than in promoting the welfare of mothers and babies. It will be

most deplorable to have our pediatric family lose well-merited prestige and respect for our past liberality of thought and conduct and for our receptiveness to new ways of furthering the health and welfare of children.

The Emergency Maternity and Infant Care program arose from tragic conditions observed and reported by physicians, public health workers, social workers and officers of the armed Services. These reports reached Congress and other governmental agencies and the necessary additional legislative action followed. The Congress freely and unconditionally gave to the fighting men—as a part of just reward and appreciation for their sacrifices—medical care for their wives and babies. No informed person questions the lift to soldier and sailor morale achieved by this action of the Congress! The Surgeons General of the Army and Navy have so testified publicly! If there be opposition to the main purposes of the program, criticism must be directed toward the Congress.

Responsibility for the administration of the Emergency Maternity and Infant Care program was lodged in the Children's Bureau where certain policies and decisions had to be made, which naturally were subject to controversy. As in all human undertaking mistakes were made—few, in my opinion, considering the magnitude of the task, the newness and intricacies of the problems involved, the nature of the Congressional mandate, and the urgency of the situation under war conditions. But let the prime fact concerning the Emergency Maternity and Infant Care program be squarely faced—*the job was, on the whole, well done*—a fact appreciated by the public, by the beneficiaries, by the fathers in the Armed Services!

It was for the sake of soldiers, sailors and their families that the Emergency Maternity and Infant Care program was conceived and administered; pediatricians, obstetricians, and health officials share with the Children's Bureau in the success of a great humanitarian venture. It was not the purpose of the program to change medical practice in the United States; but, the primary mission fulfilled, no one can foretell the character or extent of the program's influence on the future pattern of medicine.

No one should be satisfied with the distribution of medical care in the United States and no one knows the complete solution of the various problems involved. We are not wise enough to foretell the exact course of pediatric practice in the world-wide reorganization of society in which we in America must participate. We believe our future role may well be determined more by forces outside the pediatric group than from within it. There are many persons who believe the people through their government have the right to a voice in determining the kind of medical care they are to receive. Only if we are alert to new concepts and procedures and eager for experimentation in medical practice as in the laboratory will we be able to give effective counsel and guidance.

In the Emergency Maternity and Infant Care program, through fortuitous circumstances, we have been presented with an experimental study of a segment of the medical care problem, well defined and clearly limited. Shall we discard valid experimental data thrown in our laps, so to speak, by the exigencies of war or shall we welcome the opportunity to salvage something constructive from the holocaust! And would it not be ungrateful, short-sighted, and unscientific, contrary to our own high purposes and, above all, against the best interests of America's children to cease collaboration with our experienced Children's Bureau friends—tried and true crusaders in our common cause of maternal and child welfare—because of blind fears of the impact which the Emergency Maternity and Infant Care program may have on the course of pediatric practice; the course is bound to change sooner or later, Children's Bureau or no Children's Bureau, transference of health activities to the Public Health Service or otherwise! Rather would it not be the part of wisdom and medical statesmanship to continue our support of and collaboration with the Bureau as counsellors and advisors in this day of its most widespread usefulness, appreciation, and responsibility! As with all governmental agencies, the policies of the Children's Bureau are subject to review and modification.

American pediatrics has a glorious record of scientific achievement, an enviable reputation for unselfish public service, an eager appreciation of the fact that "new occasions teach new duties"! Let us by no overt act place a "blot in the 'scutcheon" of our heritage!

Grover F. Powers, M.D.

The Pediatrician and the War

The following is a continuation list of the Fellows of the American Academy of Pediatrics on active duty in the Military Services:

Army

Dr. Carl J. Oehs, Cincinnati, Ohio (Captain, Air Force)
Dr. Peirce D. Knott, Sioux City, Iowa (Captain)

Navy

Dr. Wesley R. Heard, Pasadena, Calif. (Lieutenant Commander)
Dr. Frederick P. Rogers, West Hartford, Conn. (Lieutenant Commander)

United Nations Relief and Rehabilitation Administration

Dr. Stanton Garfield, Concord, Mass.

United States Public Health Service

Dr. Samuel Hurwitz, San Francisco, Calif. (Passed Assistant Surgeon)

The following Fellows of the Academy have been promoted since entering the Military Services:

Army

Lieutenant Horst A. Agerty to Captain
Captain Lawrence C. Baehmann to Major

Navy

Lieutenant Benjamin Spock to Lieutenant Commander

United States Public Health Service

Passed Assistant Surgeon (R) Samuel J. Nichamin to Surgeon (R)

Lieutenant Commander Samuel J. Levin United States Navy, has returned to private practice at 469 Fisher Building, Detroit 2, Mich.

News and Notes

The *American Pediatric Society* will hold its annual meeting at the Claridge Hotel, Atlantic City, September 25, 26, and 27, in connection with The Association for Pediatric Research.

Dr. Henry J. Gerstenberger, Director of the Babies and Childrens Hospital in Cleveland and Director of Pediatrics of the Western Reserve Medical School has been granted a leave of absence by the University Trustees to permit him to devote his time to writing and publishing the results of his experimental work over a number of years. He will retain his title of Professor of Pediatrics.

Dr. John A. Toomey has been appointed Acting Director of the hospital and Acting Director of Pediatrics in the medical school.